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HISTAMINE*

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Histamine has attracted much attention because it has dramatic pharmacological effects in very small doses and because it is widely distributed in animal tissues. These two fundamental facts were clearly established by Dale and his colleagues between 1910 and 1927. This early work has often been reviewed (Feldberg and Schilf, 1930; Gaddum, 1936, etc.) and will only be briefly summarized now.

Pharmacological Actions

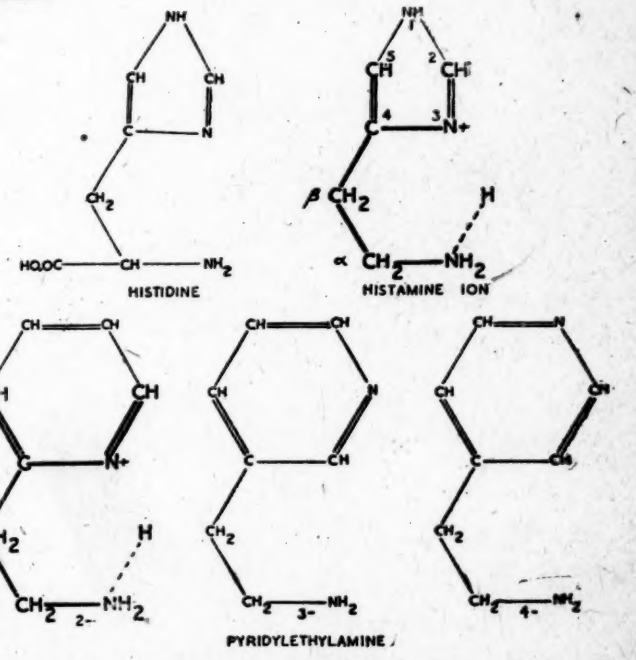
Histamine causes contraction of most plain muscle. This effect is particularly marked if the muscle comes from a guinea-pig; and this animal provides various preparations which can be used to detect histamine in concentrations down to about 10^{-7} or 10^{-8}. If a high concentration is left in contact with the muscle the contraction is not maintained. The muscle relaxes, although still in contact with histamine; even after the solution has been changed the muscle remains for a time insensitive to further applications of histamine though still sensitive to other drugs.

The contraction of plain muscle is well shown in isolated preparations and also when histamine is injected intravenously. In some species of animals large doses kill by this action, but the form of death varies, probably owing to differences in the distribution of the plain muscle. Guinea-pigs are killed by the action of histamine on the bronchi; rabbits by its action on the pulmonary arteries; and dogs by its action on the hepatic veins.

In some animals, including cats and men, histamine has a powerful action on the capillaries, which dilate. This is well shown by injecting histamine into skin, when it produces the well-known triple response which is called urticaria because of its resemblance to the effects produced by the sting of a nettle. The simple explanation of this resemblance has recently been discovered by Emmelin and Feldberg (1947), who find that nettle-stings actually contain histamine in a concentration of about 0.1% together with acetylcholine in a concentration of 1%. The urticaria is due to the histamine, and the pain is due to the two drugs acting together. The intradermal injection of either of them alone is painless.

When large doses of histamine are injected intravenously in cats the capillaries dilate so much that the blood pressure falls to very low levels, and so much plasma leaks out that the blood becomes very concentrated. These changes are the cause of death in cats. Histamine thus causes a form of shock which has much in common with shock due to other causes. The enthusiasts concluded that shock was always due to the release of histamine, but they were certainly wrong; there are many kinds of shock.

When histamine is injected subcutaneously, so that it is slowly absorbed, the mucous membrane of the stomach secretes large quantities of acid juice poor in enzymes. The use of this fact as a test of gastric function is the main clinical application of histamine. Histamine also stimulates the lacrimal glands, the salivary glands, the pancreas, and the glands of the intestine, but not the sweat glands.



Histamine is a base (β-iminazolylethylamine) which can be obtained from histidine by decarboxylation. It is soluble in water and ethyl alcohol, but not in ether. It can be extracted from alkaline watery solutions by various solvents such as amyl alcohol and re-extracted from the amyl alcohol with acid. It is extremely stable in acid solutions. When titrated with acids it shows two dissociation constants corresponding to *p*H 5.9 and *p*H 9.7 (Levy, 1935). Under physiological conditions it therefore behaves as a univalent cation. According to Niemann and Hays (1942), the structure of this cation is as shown above. Ionization is associated with the uptake of a proton attached to the amine group by means of a hydrogen bond (shown by a dotted line) and chelation occurs, which means that an unstable ring is formed.

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Histamine may be adsorbed in two different ways (see diagram). Adsorption on charcoal is increased when the solution is alkaline; this is presumably because charcoal adsorbs the free base (Phelps and Peters, 1929). On the other hand, adsorption on fuller's earth or magnesium trisilicate is increased when the solution is acid; this is presumably because these substances adsorb histamine ions in exchange for other cations.

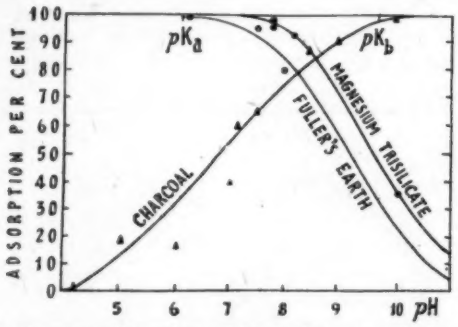


Diagram showing adsorption of histamine. In alkaline solutions adsorption on charcoal is increased, but adsorption on fuller's earth or magnesium trisilicate is decreased.

Several workers have studied the pharmacological activity of methylhistamines. Vartiainen (1935) found that if one methyl group is attached to the amino-nitrogen the resulting compound is more active than histamine in some tests and less active in others. If two methyl groups are attached to this group the compound still has histamine activity, but is less active. If three methyl groups are attached the compound becomes a quaternary base which acts like nicotine and has no histamine activity. Alles, Wisegarver, and Shull (1942) studied the compound formed by attaching a methyl group in position α. This compound has very little histamine activity; the most interesting thing about it is that it is not attacked by the enzyme histaminase (or diaminoxidase). They point out that this effect is similar to that of attaching a methyl group in the corresponding position in sympathomimetic amines, which are thus protected against aminoxidase.

There are three possible pyridylethylamines, depending on the position of the side-chain in the pyridine ring. The compound whose formula is shown above (2-pyridylethylamine) has effects like those of histamine and is almost as active. It is therefore suggested that the essential group for histamine activity is that shown large [CH : NC(CH_2.CH_2.NH_2) : CH]. The other two pyridylethylamines do not contain this group and do not act like histamine. Their pharmacological effects are like those of sympathomimetic amines, whose essential structure is phenylethylamine. In these compounds the pyridine ring behaves as if it were a benzene ring (Walter, Hunt, and Fosbinder, 1941; Niemann and Hays, 1942).

Antihistamines

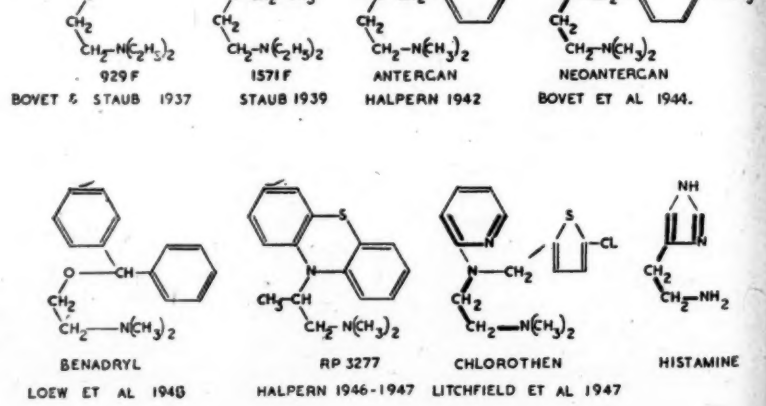
(Bovet and Walthert, 1944; Feinberg, 1946; Loew, 1947.) It has long been known that many of the pharmacological effects of adrenaline are opposed to those of histamine. These two substances act as physiological antagonists, and the body uses them as such. The injection of histamine releases adrenaline and, according to Staub (1946), the injection of adrenaline releases histamine. He found that, when 0.2 mg. of adrenaline was injected intravenously in man in nine minutes, the plasma histamine rose from 10 to 150 μg. per litre. This work seems to confirm a suggestion made long ago by Dale, who thought that the vasodilator effect of small doses of adrenaline might be due to release of histamine. Experiments which appeared to show that adrenaline did release histamine from the lungs turned out to be inconclusive (Dale and Richards, 1927), but the work of Staub supports the theory on which the experiments were based.

Another class of substance which is opposed to histamine comprises the substances that destroy it. Formaldehyde (Kendall, 1927) destroys histamine *in vitro* and may oppose its actions on an isolated organ. According to Garan (1938) CO_2 has a similar action, possibly due to the formation of a carbamino compound. Nitrites also destroy histamine *in vitro* (Gaddum and Schild, 1934). There is no evidence that they do this *in vivo*; if there were, it might explain the fact that nitrites inhibit smooth muscle. The enzyme histaminase is presumably the main factor which does destroy histamine in the body; but it seems to be ineffective when injected, and it is difficult to see how it can possibly be effective by the mouth (cf. Feinberg, 1946).

It is possible to immunize the body against histamine by injecting an antigen prepared by coupling histamine to a protein (cf. Feinberg, 1946). This discovery would have made more stir than it did if it had not been overshadowed by the discovery of drugs which probably act as competitive antagonists, combining with the tissues in the same way as histamine and keeping the histamine off.

Perhaps the first competitive antagonist that should be considered is histamine itself. Its power of desensitizing tissues to its own action has already been mentioned. In the search for other antihistamines Edlbacher, Jucker, and Baur (1937) tested most of the amino-acids and found that histidine, arginine, and cysteine had some effect on high concentrations. It seems natural that histidine should act in this way as its molecule differs from that of histamine only by the presence of a carboxyl group. The molecule of arginine can be drawn to look like that of histamine, but it is not so easy to suggest why cysteine should act in this way.

The discovery of the really potent antihistamines is mainly due to Bovet and his colleagues in the Pasteur Institute in Paris. This laboratory had been interested for some years in a series of drugs with an action antagonistic to adrenaline (Bovet, 1943). The molecules of adrenaline and its allies contain phenylethylamine. The anti-adrenalines studied in Paris were tertiary amines containing phenoxyethylamine. The introduction of oxygen between the benzene ring and the side-chain, together with the attachment of alkyl groups to the amino-nitrogen, seemed to convert drugs which acted like adrenaline into drugs which opposed adrenaline. Ungar, Parrot, and Bovet (1937) found that some of these drugs also acted against histamine. The first of the new antihistamines to attract attention was 929F, or thymoxyethyldiethylamine (Bovet and Staub, 1937). The more active drugs discovered later were mostly modifications of this original substance. The formulae of some of these substances are here shown.



In 1571F (Staub, 1939) the oxygen in 929F is replaced by NC_2H_5 and thymol by phenol. In "antergan" (Halpern, 1942) the NC_2H_5 is replaced by $N.CH_2.C_6H_5$ and the diethylamine group is replaced by dimethylamine. In "neoantergan" (Bovet *et al.*, 1944) the benzene ring is replaced by pyridine, and a methoxy group appears. This interesting drug is also known as pyranisamine or "anthisan." "Pyribenzamine" has just the same molecule as neoantergan except for the absence of the methoxy group.

A large number of other antihistamines have been synthetized in the last few years, including benadryl, "antistin," chlorothen, RP 3277, hetramine, and others, but neoantergan appears to be more active and specific than most of the other antihistamines which have been discovered more recently.

Various theories have been advanced to explain the action of these drugs, but the most probable is that they act by competition, blocking up the sites of action of histamine. The results of quantitative studies of the antagonism are compatible with this view. The slope of the logarithm of the dose-effect curve appears to be unaltered by antihistamines (Schild, 1947b). The antagonism between benadryl and histamine seems to be simple (Wells *et al.*, 1945). Halpern and Mauric (1946) have studied the antagonism between antergan and histamine and got more complex curves, but their results can be fitted by a formula of the type proposed by A. J. Clark (1937) to express the relationship in the case of other drugs which are thought to act by competition.

Bovet believes that not only the antihistamines but anti-adrenalines such as phenoxyethyldiethylamine act in this way. It has been objected (Loew, 1947) that the molecules of antihistamines are so different from those of histamine and from one another that they would not be expected to combine with the same groups in tissues. The manner in which the above formulae are drawn represents an attempt to answer to this objection. It has already been concluded from the study of the pyridylethylamines that the essential pharmacodynamic group of histamine is the skeleton shown in thick lines in its formula. Neoantergan contains this skeleton, but the two parts of it are separated by a nitrogen atom with other groups attached to it. This separation of the side-chain from the ring is comparable with the similar separation in the molecules of the synthetic anti-adrenalines. It is noteworthy that the nitrogen in the ring in neoantergan is in the same position as it is in histamine. Several other powerful aintihistamines, such as pyribenzamine, hetramine, and chlorothen, contain a nitrogen in the same position. Some of the other molecules do not fit into this picture quite so well, but none of them are so widely different from neoantergan as to disprove the theory of competitive antagonism. This is not, however, the only possible theory.

These antihistamines appear to antagonize all the actions of histamine, with the notable exception of its action on the gastric juice, which is little, if at all, affected. Their activities have been measured in various ways, the most satisfactory being probably that proposed by Schild (1947a), according to which the activity is expressed in terms of the pA_2—the negative logarithm of the molar concentration which is just sufficient to make the tissue half as sensitive to histamine as it was before. Using guinea-pig's intestine, Schild measured the pA_2 for neoantergan, benadryl, pethidine, and atropine acting against both histamine and acetylcholine. Reuse (1948) has confirmed Schild's results for neoantergan and also obtained estimates for antergan, antistin, and RP 3277. These results agree with those of other workers obtained by different methods in showing the outstanding activity and specificity of neoantergan. Most of the antihistamines are fairly powerful antagonists for acetylcholine; many of them have a local anaesthetic effect and mixed effects on the central nervous system, which is depressed in man but excited in most other animals (Loew, 1947).

Other substances found to have some antihistamine action include peptamines containing histamine (Rocha e Silva, 1943), iminazole (Morris and Dragstedt, 1945), picrotoxin (Anrep *et al.*, 1939), and nicotinamide (Halpern and Daïnow, 1944).

Antihistamines can provide evidence for or against theories which attribute physiological changes to the liberation of histamine. Such evidence is of real value only when one of the more specific drugs such as neoantergan is used. Experiments of this type support the view that many of the phenomena of anaphylaxis are due to the release of histamine. On the other hand, benadryl has been found ineffective in protecting animals against trypsin (cf. Loew, 1947). This does not invalidate the evidence that trypsin liberates histamine, but does suggest that its actions are not all due to the release of histamine.

The Estimation of Histamine

Practically all our knowledge of the behaviour of histamine in the body is based upon biological assays. Colorimetric methods have been devised, but they have been found to be comparatively laborious, insensitive, and unspecific. In the early work histamine was generally detected by its effect on the cat's blood pressure, but the favourite test to-day depends on the guinea-pig's intestine. Other suitable tissues are the guinea-pig's uterus or bronchi, the hen's rectal caecum, and the human skin. In all such tests the extract of the tissue is compared with a solution of histamine and the doses adjusted until the two solutions cause equal effects. For really accurate assays the size of the effects can be measured and the result calculated statistically (Schild, 1942).

Crude tissue extracts contain many pharmacologically active substances besides histamine, and when such extracts are used the result means very little. At one time it was customary to use such extracts and to speak vaguely of histamine-like substances. The introduction of improved pharmacological techniques has made these tests more specific, and if proper precautions are taken it is now possible to be reasonably certain that the result of an assay does give an estimate of the concentration of histamine itself.

In order to do this it is necessary to subject the extract to chemical or physical procedures which remove or destroy all other substances that would affect the test. The estimation is thus comparable with a colorimetric estimation in which tissues are ashed or extracted before the final test is applied. In a method which Barsoum and I (1935a) devised in Cairo for the assay of histamine the tissue is minced and extracted with trichloroacetic acid, which precipitates the proteins. The trichloroacetic acid is removed from the extract with ether, and strong hydrochloric acid is then added and the mixture boiled for 1½ hours. This destroys other substances, and generally gives a pharmacologically pure solution after the HCl has been evaporated off. This extract is tested in comparison with histamine on guinea-pig's ileum. We found that when the concentration of histamine was very low there was enough potassium in this final solution to interfere with the test, so we devised a technique involving alcoholic extraction to get rid of this potassium when necessary. Code (1937a) improved this method by the discovery that extraction with ether was unnecessary because the HCl destroyed the trichloroacetic acid. Since then various other methods of extracting histamine for pharmacological tests have been used (cf. Minard, 1940; McIntire *et al.*, 1947).

By such methods it is generally possible to obtain pharmacologically pure extracts, but until confirmatory tests are made it is unsafe to assume that this result has been achieved. The best confirmatory test is to make parallel quantitative assays. The extract is compared quantitatively with histamine by several different methods. If all the results agree quantitatively it is probable that they give an estimate of histamine (cf. Chang and Gaddum, 1933). Histamine can be distinguished from N-methyl-histamine in this way; the methods used so far would not distinguish it from N-dimethyl-histamine.

The effects of antihistamines can also be used in evidence, provided that the experiment is properly designed.

Large amounts of antihistamines will desensitize tissues not only to histamine but also to other substances such as acetylcholine and potassium. The effect of antihistamines is therefore convincing only when they antagonize extracts in the same concentrations that they antagonize histamine. One sound way of arranging the experiment is to obtain a series of equal responses of the guinea-pig's gut with the extract and with histamine given in alternate doses. A small concentration of neoantergan is then added to the bath for a minute and the alternate dosing continued. The result is that the response to histamine is greatly depressed or abolished and then gradually recovers as successive doses are given. If the active principle in the extract is histamine its effects will be depressed to the same extent and for the same time as the effects of the standard solution of histamine. This type of test can be used to distinguish histamine from many substances, but Schild (1947b) has shown that it does not distinguish histamine from N-methyl-histamine, although these two substances can be differentiated by the method of parallel quantitative assays. This result suggests that antagonists can be used to distinguish between drugs acting at different sites in tissues but not between two drugs which act at the same site.

Evidence for the identification of histamine in extracts can also be obtained by exposing the extracts to various solvents, and destructive agents such as histaminase; but it must be remembered that this enzyme has not been prepared in the pure state, and that preparations containing it may contain other enzymes as well. Evidence depending on the use of this enzyme is not conclusive by itself.

Behaviour of Histamine in the Body

It seems likely that the histamine in the body is derived originally from histidine by decarboxylation. Histidine is one of the essential amino-acids, and it is generally supposed that the iminazole group which it contains is not synthetized in the animal body but absorbed from the intestine. Histidine may be converted into histamine by bacteria either in the food before it is eaten or possibly in the intestine. When animal tissues are eaten they also often contain histamine derived from the animal. Histamine is absorbed by the mucous membrane in the mouth, but most absorption occurs in the ileum. However, large doses may be eaten with surprisingly little effect, for reasons to be discussed later.

Histamine may also be formed from histidine in the body by the enzyme histidine decarboxylase (see Blaschko, 1945), which is present in the liver and kidneys of certain small animals. It is not known what proportion of the histamine normally present in the body is derived from this source and what proportion is absorbed from the intestine, but the fact that histidine decarboxylase appears to be absent in many species of animal suggests that it does not play an important part in providing the body with histamine.

Numerous estimates have been made of the amounts of histamine in animal tissues, with varying results (Feldberg and Schilf, 1930; Gaddum, 1936; Rocha e Silva, 1946; etc.). There are usually particularly large amounts in the lungs and skin, but most tissues may contain quite large amounts in some species at some times. The blood has attracted particular attention because it is easy to obtain successive samples of it. Most of the blood histamine is in the cells. The plasma usually contains so little that it is difficult to estimate it, but some does seem to be there in a pharmacologically active form. Emmelin (1945), for example, took pairs of guinea-pigs of which one normally had a high concentration of histamine in its plasma and the other a low concentration. When he established a cross-circulation between two such guinea-pigs bronchoconstriction occurred in the animal with an initial low plasma histamine and not in the other animal. This experiment seems to show that the concentration in the plasma does play a part in regulating the normal functions of the body. Code (1937b) came to the conclusion that most of the blood histamine is in the granulocyte cells. This view was confirmed by the fact that in myeloid leukaemia when the number of granulocyte cells was very high the blood histamine reached astronomical proportions. Later work suggests that this is not true of all species of animal and that most of the histamine in rabbit's blood is in the platelets (Minard, 1940). In any case, estimations of total blood histamine are often difficult to interpret; a fall of blood histamine may be due to the disappearance or destruction of histamine-containing cells.

Observations on the blood histamine are also complicated by the fact that when histamine is liberated into the blood by one organ it may be rapidly absorbed, destroyed, or excreted by another. Anaphylaxis in rabbits causes a fall in the histamine content of the lungs, spleen, and blood, and it is not known what happens to the histamine in these circumstances. The injection of histamine itself in rabbits has been found to cause a fall in the blood histamine apparently due to the loss of leucocytes or platelets (Rose and Browne, 1941). Such observations help to explain why estimations of histamine in the blood have not led to as rapid advances in the study of histamine as seemed possible at one time.

It has long been obvious that the histamine in the tissues cannot all be free; something prevents it acting under normal conditions. If all the histamine in a cat's lungs were liberated it would kill the cat. The methods generally used for the estimation of histamine do not estimate free active histamine but only the total amount that can be extracted from the tissues. When tissues are ground up in saline part of the histamine is released, but part of it appears to be bound to cellular debris, from which it can be released by procedures, such as heat, which coagulate the proteins (Trethewie, 1938).

When histamine is injected intravenously most of it disappears from the blood within a minute or two and is taken up by the tissues and particularly by the kidney (Rose and Browne, 1938; and cf. Emmelin, 1945). Various alkaloids disappear from the blood equally quickly. It is unlikely that this phenomenon is entirely due to the combination of the drug with the specific receptors on which it acts. It is thus probable that histamine can combine with tissues in at least two ways, one of which is specific and produces pharmacological effects, and the other of which is unspecific and merely removes the drug from the blood. According to Phelps (1935) the pharmacological effects depend on the combination of free histamine base with the tissues, and according to Rocha e Silva (1946) the unspecific combination of histamine with the tissues depends on a mechanism which will be discussed later. But first consider the factors which release histamine from the tissues.

Release of Histamine from Tissues

A number of different methods have been used to study this question. Lewis (1927) showed that various injurious agents produced effects which could be attributed to the release of histamine or something like histamine. The best-known of these effects is the local triple response produced in the skin by intradermal injections, but Lewis and his co-workers also observed other effects such as vasodilatation in the skin of the face which could be attributed to the release of histamine into the general circulation (Lewis and Harmer, 1927). Various other similar methods have been used; for example, the released histamine has been detected by its effect on the gastric juice (Kalk, 1929;

Ungar, 1935; Feldberg and Holmes, 1941) and on the blood pressure (McIntosh and Paton, 1947).

In some experiments the evidence has been the demonstration of a general rise of the histamine content of the circulating blood (Dragstedt and Mead, 1936) or of the blood coming from one particular organ (Anrep and Barsoum, 1935) or in the lymph (Dragstedt and Gebauer-Fülnegg, 1932). The release of histamine can also be demonstrated in tissues such as guinea-pig's lungs perfused with salt solutions (Bartosch, Feldberg, and Nagel, 1932) or by diffusion from tissues suspended in salt solutions (Schild, 1939) or from blood cells into plasma (Katz, 1940). Another possible method, to be discussed later, depends on estimating histamine in the urine.

The factors which control the release of histamine have recently been reviewed by Kellaway (1947), and it will therefore be unnecessary to discuss all the details here.

Histamine is liberated by trypsin, and this fact has been made the basis of an interesting theory regarding the way in which histamine combines with tissues. Rocha e Silva (1946) showed that crystalline trypsin liberates histamine from lungs or from blood cells. It has been shown by Bergmann that crystalline trypsin is a much more specific enzyme than had been supposed, and that it acts on the peptide links formed by the carboxyl groups of the basic amino-acids lysine and arginine. Rocha e Silva therefore suggests that the amine group in histamine combines with the carboxyl groups in these two acids, which themselves presumably form part of protein molecules in the tissues. In support of this very definite theory he finds that chymotrypsin, which attacks the carboxyl group of aromatic amino-acids, does not liberate histamine from cells. On the other hand, papain, which contains a mixture of proteolytic enzymes, does liberate histamine (Rocha e Silva and Andrade, 1943). There is evidence that proteolytic enzymes are liberated or activated in various forms of injury. This is one mechanism by which histamine may be released.

Rocha e Silva (1946) has suggested a theory of how this happens. It is well known that histamine is released in anaphylactic shock, together with other substances such as heparin (Feldberg, 1941; Dragstedt, 1941; Rose, 1947). At the same time leucocytes and platelets disappear from the blood. Rocha e Silva found that both peptone and extracts of ascaris caused similar effects in dogs, and obtained microscopical evidence that the leucocytes and the platelets were retained in the liver. He believes that these cells liberate or activate trypsin, or some similar enzyme, in the tissues and that this trypsin then liberates both histamine and heparin. Such experiments are complicated by the fact that heparin antagonizes the action of trypsin (Rocha e Silva, 1945).

A large number of other substances are known to liberate histamine, and it is clear that they do not all act in the same way. The effects of various forms of injury have been studied in detail by Feldberg, Kellaway, and their co-workers in Australia (Kellaway, 1947), who found that a number of different irritant poisons had various effects in common. The poisons studied included snake venoms, bee venom, peptone, toxins from staphylococcus and *Clostridium welchii*, and mercuric chloride. All these poisons caused a liberation of histamine, and some of them the liberation of other substances as well. For example, cobra venom also liberated adenosine compounds, which inhibit most smooth muscle, and a substance which causes a slow contraction of guinea-pig's isolated intestine and is known simply as the "slow-reacting substance." Another important substance liberated by cobra venom is lysolecithin, which is formed from lecithin by an enzyme. This substance is itself destructive of cells, causing haemolysis and the release of proteins, pigments, histamine, and small amounts of the slow-reacting substance (Feldberg and Kellaway, 1938). Some, at least, of the release of histamine by cobra venom must be the secondary result of the formation of lysolecithin.

Histamine is also liberated by various substances which do not produce obvious injury. For example, Alam *et al.* (1939) showed that curare liberates histamine, and this fact has been confirmed in experiments with tubocurarine (Schild and Gregory, 1947; Grob *et al.*, 1947). McIntosh and Paton (1947) have also found that stilbamidine and a series of other diamidines as well as diamines and diguanidines also release histamine in the body.

In most of the experiments discussed so far there was no question of any new formation of histamine. The appearance of histamine in the fluids in contact with tissues has often been shown to be accompanied by a disappearance of similar amounts of histamine from the tissues themselves. The work of Dekanski (1945) suggests that some other mechanism may play a part in the effects of the exposure of tissues to high temperatures. In the hope of following the fate of histamine liberated by injury he made extracts of whole mice. Anaesthetized mice were immersed in water at 60° C. for 10 or 30 seconds. During the first hour after this treatment the total amount of histamine which could be extracted from the whole body rose from an average value of 216 μg. per mouse to about double this value. The main site of this new formation of histamine appeared to be the skin, but it is not known from what precursors the histamine was formed.

The Fate of Histamine

Histamine is destroyed by some bacteria and also by the enzyme histaminase which is present in the body (Best, 1929). According to Zeller (1938, 1941) this same enzyme also destroys various diamines, such as putrescine and cadaverine, and should therefore be called diaminoxidase. The enzyme is inhibited by cyanide and acts by oxidation. One atom of oxygen is absorbed and one molecule of ammonia is formed when one molecule of histamine is destroyed by the purified enzyme; H_2O_2 is formed and the iminazole ring is destroyed. The most sensitive method of estimating the amount of enzyme in a solution depends on adding histamine and following its destruction by pharmacological tests. Other methods depend on the measurement of the oxygen consumption, the ammonia production, and the peroxide production.

The highest concentrations of the enzyme are in the intestinal mucous membrane, the kidney, and the placenta. The liver contains surprisingly little. In normal circumstances the blood contains very little, but during pregnancy there is an enormous increase of the histaminase content of the blood of women. This phenomenon was first described by Marcou (1937) and has been confirmed by many others (for references see Ahlmark, 1944; Anrep *et al.*, 1947). The enzyme is thought to come from the placenta.

Kapeller-Adler (1944) studied this phenomenon by means of a colour test depending on the formation of H_2O_2. The rise in the concentration of the enzyme in the blood during normal pregnancy could be demonstrated by this test when either histamine or cadaverine was used as substrate, but bloods taken from women suffering from eclampsia or pre-eclamptic toxaemia behaved in a curious way. The effect of these bloods on cadaverine was similar to that of blood from normal pregnant women, but their effect on histamine was much less. This observation seemed at first to suggest that the enzyme oxidizing cadaverine was

not, after all, identical with the enzyme oxidizing histamine. The evidence on this point has therefore been re-examined using the Warburg technique to measure the oxygen consumption as well as other tests. A highly purified preparation of the enzyme from pig's kidney was used in this work. The results showed that there were not two independent enzymes. When histamine and cadaverine were both present the combined effect on the oxygen consumption was less than the sum of their effects when either is present without the other. Cadaverine inhibited the destruction of histamine as measured by biological assay. The effects of various poisons and changes of *p*H produced similar effects with either substrate, but dialysis had an effect like eclampsia: it decreased the action of the purified enzyme on histamine and increased its action on cadaverine. Both these effects were reversed by flavine adenine dinucleotide; the effect of dialysis thus appears to be due to the removal of this substance. The relation of these observations to those on toxaemia obviously requires further investigation.

The eventual fate of most of the histamine in the body is probably to be destroyed by the enzyme histaminase, but a certain amount appears in the urine. The first clear quantitative evidence of this was obtained by Anrep, Ayadi, Barsoum, Smith, and Talaat (1944), who found that the activity of extracts of urine could be increased by acid hydrolysis. The histamine in the urine seems to be partly free and partly conjugated with other substances, from which it can be liberated by acid. These facts have been confirmed and extended in Edinburgh by Adam. He has been using a simplified form of the test devised by Anrep *et al.* to measure the histamine in human urine. In normal circumstances the concentration of histamine in the urine is comparable with that in the blood—about 50 μg. per litre. This is near the limit of what can be measured by the methods available. When histamine is given by the mouth to man about 1% of it appears as conjugated histamine in the urine, but when histamine is given by slow intravenous infusion it is free histamine which appears in the urine. These observations confirm results obtained by Anrep *et al.* in experiments on dogs.

The fact that large doses of histamine have very little pharmacological effect when swallowed may be partly due to this formation of conjugated histamine, but other factors may be more important. The mucous membrane of the gut contains particularly large amounts of histaminase, and this probably also plays a prominent part in protecting the body from the effects of the absorption of histamine. It has already been mentioned that other organs, such as the kidney, also contain histaminase, and the general result is that only a small amount of histamine normally appears in the urine. This proportion may be much greater when large doses of histamine are given. This is well shown in some experiments by Alexander (1944), who injected 3 mg. of histamine intravenously into each of a group of mice, and then followed its fate by estimating it in the urine and in extracts of the whole mouse. The percentage appearing in the urine in these experiments varied widely, but on the average it was 37.7. After 24 hours the histamine content of the mice had fallen practically to the normal value of 0.3 mg. per mouse, so that the other 62.3% of the histamine must have been destroyed in this time. During the first hour, when the mice were flooded with histamine, excretion in the urine was the main channel by which they got rid of it.

The main interest of estimations of histamine in the urine lies in the fact that they provide a possible means of studying the factors which cause the liberation of histamine in the body. Under the conditions of Adam's experiments there was no detectable rise in the blood histamine, although measurable quantities of histamine appeared in the urine. It thus seems likely that the liberation of histamine in the body may be followed by estimating it in the urine even when no changes occur in the blood histamine.

Histamine in Normal Physiology

It is natural to suppose that the local control of the circulation may depend on histamine. Vasodilatation is known to occur when the blood supply to a tissue is obstructed or when the activity of the tissue is increased. These phenomena may be partly due to the local release of histamine, but the evidence is conflicting. Workers in Cairo got evidence of an increase in the histamine content of blood coming from the voluntary muscles of a dog when the circulation was obstructed; when the muscles were stimulated the effect was much larger. They also did experiments with a heart–lung preparation, and found that when the heart worked harder it liberated more histamine (Barsoum and Gaddum, 1935b; Anrep and Barsoum, 1935; Anrep, Barsoum, and Talaat, 1936; Anrep, Barsoum, Talaat, and Wieninger, 1939). Some of these conclusions were supported by the results of Feldberg and Holmes (1941), who found that stimulation of voluntary muscles caused gastric secretion in cats which could be attributed to the release of histamine. Unfortunately other workers failed to confirm the experiments in Cairo (Code, Lovatt Evans, and Gregory, 1938; Emmelin, Kahlson, and Wicksell, 1941; Kwiatkowski, 1941). Emmelin and Emmelin (1947) found that benadryl in doses sufficient to reduce the effect of histamine did not reduce the reactive dilatation of the vessels in a cat's leg after occlusion of the circulation.

According to Anrep, Barsoum, Salama, and Souidan (1944) some at least of the negative results were due to the fact that the histamine is very rapidly washed away unless drastic measures are taken to control the blood flow when it is first released. It has also been pointed out that the muscles of the dogs in Cairo contained three to four times as much histamine as the muscles of the dogs used by other workers. It is possible that histamine did contribute to the hyperaemia in all the experiments, but that it was only when it was present in large amounts that it appeared in the venous blood. In any case the evidence in favour of histamine's function in the local control of the circulation cannot be regarded with complete satisfaction at present. It is very probable that various other substances are involved.

The question of the release of histamine by nerves has received less attention than it deserves. Ungar (1935) stimulated the posterior roots antidromically in dogs and found that the vasodilatation thus produced was accompanied by gastric secretion. He attributed this at first to the release of histamine into the general circulation, and suggested that these nerves should be called histaminergic. Kwiatkowski (1943) obtained more direct and convincing evidence in favour of this conclusion. He found that antidromic stimulation in cats caused the appearance of a histamine-like substance in the venous blood. Confirmatory results were obtained when a cat's leg was perfused with Tyrode's solution. High concentrations of histamine were also found in extracts of the nerves which cause these effects, and Kwiatkowski considered that this was analogous to the fact that extracts of cholinergic and adrenergic nerves contain high concentrations of the substances liberated at their endings. There are, however, various complications which suggest that the analogy is not a close one. Kwiatkowski himself found that degeneration caused

an increase in the histamine content of nerves, whereas it is known to have the opposite effect on their content of acetylcholine and sympathin. The work of Koshtojanz, Ryvkina, and Mitropolitanskaya (1945) indicates a more complicated situation. They compared the effects of a blow on the head with those of ether narcosis. Extracts of nerves taken from animals killed by this form of violence contained little or no histamine, whereas those obtained from anaesthetized animals contained large amounts. It is clear that there is still much to be learned about the histamine metabolism of nerves.

Therapeutic Applications

(Rose, 1947)

The realization that the release of histamine plays a part in various pathological conditions has stimulated the search for ways of counteracting its effects. The results of this search have already been briefly discussed; the most promising antidotes for histamine are the drugs, like neoantergan, which probably act as competitive antagonists. Their effect in anaphylaxis has led to their clinical use in allergy. They have been found effective in allergic urticaria. In various other dermatological conditions their main effect is to diminish itching. They are also effective in hay-fever and other forms of spasmodic rhinitis. There is evidence that when patients are specifically sensitive to drugs such as liver extracts or insulin the unpleasant effects can be suppressed with antihistamines and the treatment continued. Under these conditions the patient may be desensitized so that the administration of the antihistamine need not be continued indefinitely. Antihistamines may cause various toxic effects, of which the most troublesome at present seems to be drowsiness. Much work remains to be done before the full possibilities and limitations of these drugs are known, but it is already clear that they have some uses. Histamine thus provides another example of the way in which fundamental discoveries which were originally inspired by unorganized scientific curiosity may bear practical fruit which could not have been foreseen.

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A paper entitled "Some Aspects of Physique in Boys and Girls," by R. E. Roper, M.A., M.Ed., has been published (price 2s. 6d., post free) by the Research Board for the Correlation of Medical Science and Physical Education, Apothecaries Hall, Blackfriars Lane, Queen Victoria Street, London, E.C.4. Mr. Roper examined 1,852 children from State schools and day nurseries, a sample which excluded children at special schools. He has tabulated the age, height, weight, and other particulars of the physique and carriage of the children. He recommends that education authorities should consider employing chiropodists to work in schools, that special corrective classes should be available for children with minor defects, that a pair of large mirrors should be provided in all schools, that education authorities should provide travelling x-ray equipment to examine the children's physique, that each school should have a rest room for children with special needs, that physical exercise should not be omitted to provide more time for study when examinations approach, and he advocates fuller co-operation between physical education and the medical profession.

"ANTISTIN" IN DERMATOLOGY

BY

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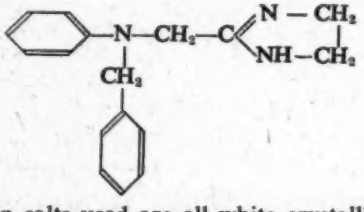
Research by K. Miescher and co-workers on antihistamines led to the synthesis of "antistin," a substance which chemically has the formula 2 N-phenyl-N-benzyl-aminomethyl-imidazoline.



The antistin salts used are all white crystalline powders. The hydrochloride, which is 2% soluble in water, is used in the tablets. The methanesulphonate is readily soluble in water, and is given parenterally. Antistin sulphate has a solubility of about 4% in water, and is employed as a local application to the mucous membrane in hay-fever.

Pharmacology

The pharmacological properties of antistin have been investigated by Meier and Bucher (1946a, 1946b) in the usual animal experiments employed to ascertain the efficacy of this type of drug. Anaphylactic symptoms were entirely prevented by previous medication with antistin in rabbits sensitized to egg albumin; antibody production appeared to be increased when elicited in conjunction with the administration of antistin; addition of antistin to the liquid in which isolated organs were immersed suppressed or prevented anaphylactic contraction (Schulz-Dale's experiment). The antagonism of antistin to histamine was shown in the isolated perfused posterior extremity of the rabbit and in the isolated intestine of the guinea-pig; the fatal consequences from histamine-induced bronchospasm in the guinea-pig were prevented by premedication with antistin. Its toxicity was found to be relatively low, and cumulative action slight. Brack (1946) demonstrated its peripheral action on the vasomotor system in man by the effects of local application in scratch-tests with histamine, diethylmorphine, and simple trauma; he observed suppression of the irritation and a reduction in the size of weal formation. Antistin did not reduce the irritation which followed the application of adrenaline in this scratch-test technique. Staub (1946) found that the temporary increase in the histamine content of the blood in man after the slow intravenous administration of 0.2 mg. of adrenaline was diminished or abolished by the previous administration of antistin.

Clinical Trials

Schindler (1946) attempted a clinical evaluation of antistin in a mixed series of conditions associated with pruritus. Among four patients suffering from jaundice due to infective hepatitis, three were relieved in one to three days, and in one there was no conclusive result. In two patients with carcinoma of the duodenum relief was obtained after two and six days' medication respectively. One patient with icterus of unknown aetiology was free from pruritus after two days' treatment. Senile pruritus was relieved in one patient, but in another, after a temporary amelioration, the drug proved ineffective. An old man with chronic generalized pruritus experienced relief only while taking antistin tablets. Itching associated with lymphogranulomata was relieved in one patient, but in another, after an initial period of partial relief, the drug proved useless. Relief was obtained after three days' treatment in a patient suffering from plasmocytoma. In a patient with carcinoma of the pancreas immediate success was followed by subsequent failure. The result of treating one patient with drug-pruritus was unconvincing.

Nine cases of acute urticaria—three of which were due to drugs, two to sera, two to foodstuffs, and one following ultra-violet light therapy—were rapidly relieved by antistin. One patient suffering from recurrent urticaria obtained speedy relief from a relapse, whereas another patient who also suffered from myocardial degeneration experienced little benefit. It proved ineffective for two patients with erythema nodosum.

Schindler found that dosage was purely empirical; he administered up to 300 mg. daily intravenously, intramuscularly, or subcutaneously, and up to 600 mg. by mouth. He tried the effect of a 200-mg. dose intravenously in a normal control. The only ill effect suffered was a sense of warmth in the head, lasting about five minutes. Doses of 300 mg. daily for 10 days in four normal controls did not produce any unpleasant symptoms, nor were the pulse, blood pressure, or respiratory rate affected. Occasionally, when the subcutaneous route was used, a painful nodule persisted for a few days at the site of injection.

Brack (1946) has carried out more extensive trials on about a hundred patients suffering from various skin disorders. Nine patients with acute urticaria and four patients with "cold" urticaria manifested rapid relief. Seven patients with chronic urticaria were improved for long periods after 2 to 3½ weeks' medication. Four patients with nervous pruritus obtained relief, whereas five other patients required ancillary measures to effect improvement. Among 17 patients with neurodermite, 12 enjoyed suppression of irritation without any apparent local change occurring in the lesion. Five patients with prurigo vulgaris were cured. Itching in lichen ruber planus, psoriasis, and after scabies also responded to antistin.

The dosage Brack used was empirical, and varied from 100–200 mg. during the night to 600 mg. by mouth through the day. It was also given by intramuscular or slow intravenous injection in doses up to 100 mg. A few patients experienced transitory faintness or dizziness, but this was avoided by reducing the dosage or retarding the rate of intravenous injection. One patient suffered tetany-like cramp of hands and fingers on doses exceeding 400 mg. daily.

Skouby (1947) treated a group of 43 patients—six with vasomotor rhinitis, 10 with angioneurotic oedema, 15 with urticaria, 12 with asthma. It proved effective in the first three groups only. Thirteen patients suffered from mildly disturbing side-effects, which in seven patients persisted during administration of the drug. Two of the latter preferred to discontinue treatment.

Britton (1947) has used it for 11 patients with urticaria, with some relief in five. Twenty among 54 patients developed unpleasant side-reactions, and in seven they were severe enough to prevent continuation of this mode of treatment. The reactions included nausea (9), drowsiness (4), faintness (3), giddiness (3), headache (2), coughing attacks (2), disorientation (1), depression (1), diarrhoea (1).

Dosage, Mode of Administration, and Control Therapy

The following results are culled from clinical experience with the drug dating from March, 1947. It has been used, mainly in the out-patient department, on some 87 cases. Administration has of necessity been given in the majority of cases by the oral route, occasionally supplemented by intramuscular injection. Dosage has generally been

increased until a therapeutic result was achieved, or toxic symptoms supervened, or a dose of 800 mg. daily had been given.

As a control for the results, the effects of substitution of dummy tablets (suitably flavoured with liq. strychnine, 1/192 gr.) and cessation of therapy were assessed. In addition, in the non-urticarial pruritic syndromes the effect of a potassium bromide sedative tonic mixture was compared with that produced by antistin.

Actinic Dermatitis.—Prolonged observation throughout an exceptionally fine summer, with the use of adequate control therapy, did not provide any clear-cut evidence suggesting clinical improvement on antistin in two patients with this disorder, though the drug was pushed to the limits of tolerance. "Benadryl" in maximum tolerated dosage proved equally ineffective.

Cheiropompholyx.—Three patients with cheiropompholyx of constitutional origin obtained no relief from their irritation on antistin 100 mg. four times a day by mouth. A similar lack of response followed the use of benadryl.

Chronic Constitutional Eczema.—Compared with adequate control measures, 12 out of 13 patients experienced a moderate amount of relief from their pruritus without any change in the progress of the local manifestations being noted. Its effectiveness did not exceed that of 10 gr. (0.65 g.) of potassium bromide thrice daily in mixture form. Seven patients had previously obtained no assessable benefit on the maximum tolerated dosage of benadryl.

Infantile Eczema.—Eight patients, ranging in age from 4 months to 6 years, unfortunately showed no evidence of relief of irritation, or improvement in the local condition. Dosage ranged from 25 mg. four times daily for a 4-months-old infant to 50 mg. four times a day in a 6-year-old child. One child, aged 2, vomited on two occasions when taking 50 mg. thrice daily; there was no recurrence of the vomiting on continuing the same dosage.

Eczematous Conditions with Oedema.—The value of antistin therapy in this group of patients proved more difficult to assess. It would have been preferable to produce a series divided into two comparable groups of patients—one treated by local applications and antistin, and a second by local measures only. Circumstances, and the relatively small number of patients, have not permitted this, but the clinical impression gained was that antistin therapy was a useful adjunct in the treatment of this group. There were nine cases.

Varicose Eczema.—A woman suffered sudden generalization, with marked oedema of face, occlusion of eyes, and very severe pruritus. Antistin was given in 100-mg. doses intramuscularly thrice daily for two days, together with the application of lead lotion to the face and zinc cream to the limbs and trunk. The irritation began to diminish in 8 to 12 hours, and the oedema and symptoms had markedly abated in 24 to 36 hours.

Constitutional Eczema.—Three patients who had suffered during a number of years from recurrent attacks of generalized eczema, with oedema of the face and occasionally the arms, were treated in the above manner. The symptoms began to subside in 12 hours, and the oedema in 24 to 36 hours. One patient stated that on previous occasions the attacks, which were treated by similar local measures only, had persisted for longer periods, the oedema generally requiring from 4 to 7 days to abate and the pruritus continuing for a further number of days.

Contact Dermatitis.—Two men, suffering from mercury and cement contact dermatitis, respectively, with swelling of the face, neck, forearms, and hands, associated with confluent vesicular eczema, showed a great reduction in the oedema, diminution of the irritation, and some regression of the eruption after 36 hours. Antistin was given in a 100-mg. dose intramuscularly thrice daily for one day, followed by 200 mg. by mouth four times a day. Again, simple local applications were concurrently used.

Two other patients suffering from a similar sensitization dermatitis, but of unknown aetiology, involving the face, responded in an equally satisfactory manner.

Erythema Multiforme.—No beneficial effect was noted in two patients with this syndrome.

Dermatitis Herpetiformis.—A man aged 78 suffering from this disorder did not obtain any relief on an arsenical mixture or 1/2 gr. (32 mg.) of phenobarbitone thrice daily. Antistin—100 mg. four times a day—induced a mitigation of this symptom, but only during administration of the drug.

Lichen Obtusus Corneus.—A woman who suffered from a patch of lichen obtusus corneus in the left supraclavicular fossa for two years had been treated by occlusion of the area, infiltration with "novocain" and "proctocaine," Grenz rays, and *x* rays, as well as the usual antipruritic local applications, but without any lasting success. Antistin, 200 mg. by mouth, was prescribed for the attacks of irritation. A certain amount of relief followed. Finally the area was infiltrated direct with 100 mg. of antistin, no previous local analgesic being given, as antistin itself has a local analgesic action. Some improvement followed, and the manœuvre was repeated in a month's time. A month later the lesion had disappeared completely, and no recurrence has been noted after four months' observation.

Lichen Planus.—Of four patients, two were almost completely relieved of the irritation during ingestion of the tablets, but two derived no benefit. One of these was a man aged 66, who complained of transient dizziness while taking 100 mg. four times a day by mouth. The actual course of the disease, and the appearance of the eruption, seemed to be unaffected.

Mycosis Fungoides.—A woman who had suffered from a generalized eczematous condition with marked pruritus for five years, and who ultimately disclosed the true nature of her disorder by developing typical nodules, confirmed histologically, obtained partial relief from her pruritus on this medication without any change in the lesions.

Pemphigus Vulgaris.—Owing to the unsatisfactory state of our knowledge in the treatment of this condition antistin was tried. Though it was administered to the limits of tolerance to two patients no improvement occurred. The effect of benadryl on one of these patients proved equally disappointing.

Senile Pruritus.—Two men, both aged 80, obtained relief, whilst under observation for four and three months respectively, on 100 mg. of antistin four times a day by mouth. A woman aged 72 found no reduction in the irritation on a similar dosage. Another man, aged 80, who obtained no benefit from antistin 100 mg. four times daily, suffered a transitory paresis of the left leg and collapsed while taking this dosage.

Pruritus Vulvae et Ani.—It was hoped that antistin would afford some relief in this condition. Among 14 patients suffering from pruritus vulvae or pruritus ani, or both, of idiopathic aetiology, none showed any consistent improvement. Neither did any benefit accompany or follow the use of benadryl in equivalent dosage.

Psoriasis.—A man aged 38 experienced considerable irritation during an exacerbation of his flexural psoriasis. Antistin afforded no relief.

Chronic Urticaria.—Sixteen patients with this disorder were treated over long periods. In 13, urticarial manifestations almost completely disappeared. In the majority this relief was noted 24 to 48 hours after starting treatment. Two more patients suffered mild undisturbing recurrences, and one other on his own assessment showed a 50% improvement. One derived no benefit. Four of these patients have been free from a recurrence for three to four months following two months' antistin therapy. Four of the persons forming this group also suffered from recurrent attacks of angioneurotic oedema. In one these gradually subsided and disappeared entirely after three months' treatment with antistin; one obtained complete relief when taking the tablets; whilst the other two still had recurrences, but these were milder and less frequent. Nine of these patients had been previously treated with benadryl. Five had developed drowsiness on their respective dosage and preferred to discontinue this treatment and retain their urticaria, Three patients who did not respond had only been given a maximal dose of 100 mg. thrice daily. One patient was equally well controlled on benadryl and "anthisan."

Urticaria Papulosa.—Six children suffering from this condition did not experience any mitigation of their itch on doses up to 100 mg. four times a day. Two children showed a reduction in the tendency to scratch. One child, aged 3, developed transient convulsions on 100 mg. three times a day. Cessation of therapy was accompanied by complete resolution of this disturbing symptom.

Surveillance and Investigations

Twenty-three patients had serial blood counts performed during two to three months' therapy. No significant variations were noted. Seventeen patients had serial blood-pressure estimations performed in the out-patient department over a similar period; six of these were over 70 years old, with arteriosclerosis and mild systolic and diastolic hypertension. Antistin therapy did not appear to cause any permanent significant alteration in the readings. Repeated urinalysis in 30 patients without albuminuria or glycosuria initially did not reveal the development of either during the course of treatment.

Discussion

Antistin is one of the three antihistamine substances available in Great Britain at the moment, the other two being benadryl and anthisan. The indications for the use of the first two in dermatology are, in my experience, identical, and there is little to choose between them in efficacy. One feature concerning the effects of benadryl therapy has repeatedly been observed—notably its high percentage of toxic manifestations which, though mainly mild, are sufficient to limit its sphere of usefulness. Among 120 patients Stroh (1946) found that 14.2% suffered from undesirable side-effects. Slater and Francis (1946) recount an incident in which the driver of an electric truck lost control over his machine while taking benadryl. Nervousness, incoordination, and epileptiform convulsions occurred in a child aged 3½ years who was being treated for hay-fever (Weil, 1947). Of McElin and Horton's (1945) patients 60% complained of sleepiness, 16% of dizziness, and 14% of nervousness. Koelsche, Prickman, and Carryer (1945) state that 25 among 83 patients complained of drowsiness. O'Leary and Farber (1945, 1946) noted that 33% of their patients suffered from toxic reactions. Friedlander (1946) found a similar incidence of side-effects. Again, among 696 patients treated with benadryl, 366 instances of drowsiness occurred (*Ann. Allergy*, 1946).

In view of its somnolent and depressing effect I am reluctant to order benadryl for the motor driver, the skilled mechanic and operator, or others daily performing potentially dangerous tasks requiring a high degree of mental alertness and co-ordination. In my experience antistin has given equally good therapeutic results with a much lower incidence of untoward reactions.

There is, however, only a limited field of usefulness for this type of drug in dermatology; they effect a symptomatic alleviation, but not a cure. Those marketed to date may all cause immediate unpleasant side-reactions, and their remote toxicity has yet to be fully assessed. In some instances the amount of relief afforded justifies their use; in other disorders the same, or greater, relief can be obtained by well-tried, innocuous, and cheaper methods. In my experience, indications for the use of antistin are as follows:

1. *Urticaria and Angioneurotic Oedema.*—It affords marked symptomatic relief in the treatment of this condition while specific or non-specific curative measures are being used. It is often useful in reducing the polysusceptibility of certain skins when testing by scratch or intradermal methods.

2. *Eczematous Conditions with Oedema.*—It offers a useful addition to the dermatologist's armarium for expediting recovery.

3. *Itching in Other Skin Conditions.*—Occasionally it may prove helpful for mitigation of itching when the usual methods prove ineffective.

Undesirable Reactions

The following table reveals the incidence of unwanted manifestations found among 87 patients.

Symptoms	No. of cases
Dizziness and lightheadedness	10
Vomiting	1
Convulsions	1
Collapse	1
Disorientation	1
Local induration and soreness (29 injections)	3

No patient was prevented from obtaining benefit from this medication by the occurrence of minor untoward symptoms. If improvement occurred together with toxic manifestations a reduction in dosage relieved the unwanted symptoms without affecting the desired result.

The child who developed convulsions on 100 mg. three times a day by mouth also had threadworms, but on cessation of antistin therapy without treatment of her worms she suffered no recurrence. I am unable to state whether the heavy dosage of antistin was the sole cause of the convulsions or an additional factor to the worms in producing convulsions, or whether the child was a potential epileptic who was stimulated to the convulsing threshold by this medication. After this incident I did not give more than 200 mg. daily to a child of this age.

The only instance of vomiting noted was in a child aged 2 years receiving 150 mg. by mouth daily. It occurred on two occasions after taking half a tablet, but during the course of subsequent unreduced therapy there was no recurrence.

The patient who collapsed was a man aged 80 with arteriosclerosis in his brachial, radial, and retinal vessels, and a blood pressure of 170/95. He appeared amazingly fit, both mentally and physically, but whilst out walking suddenly fell in the street, with a sensation of having lost the use of his left leg. There were no other associated symptoms. He was aided home and recovered completely within half an hour. I saw him two weeks after the incident, and there was no evidence of any impairment of his nervous system. His pruritus had been unrelieved.

Nocturnal disorientation occurred in a man aged 76 on three occasions about an hour after taking his evening dose of 100 mg. of antistin by mouth. He was suffering from generalized eczema and had arteriosclerosis with a fairly constant blood pressure around 140/85. On one occasion he was found wandering aimlessly in a dazed condition round the ward.

It is to be noted that the major ill effects occurred either in extreme youth or in extreme age.

Summary

The effect of antistin on a number of skin diseases has been noted. It afforded symptomatic relief in urticaria and angioneurotic oedema, in some eczematous eruptions with oedema, and occasionally in other itching dermatoses. Sometimes it produced the desired result when benadryl failed. Undesirable side effects occurred in 14 out of 87 patients—a relatively low incidence for this type of drug at the present time. The only serious undesirable secondary symptoms occurred either in early childhood or in the very old.

I wish to thank my numerous colleagues who kindly referred their patients to me, and Mr. A. R. G. Chamings, of Ciba, Ltd., who provided the drug and much useful information.

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"ANTHISAN" IN TREATMENT OF ASTHMA AND HAY-FEVER

BY

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The unpredictable fluctuations which are a feature of the clinical course of asthma, together with the dauntless optimism with which asthmatics invariably welcome any new remedies, have always made clinical evaluation of these a matter of great difficulty. The very large number of initially encouraging reports of numerous different remedies in the past, now often totally abandoned, point reproachfully to the ease with which both doctor and patient are frequently mistaken in their estimate of the benefit conferred by the new preparation. It should be the duty of those who are interested in the treatment of asthma to assess as accurately as possible each new remedy, not only to protect practitioners and prevent disappointment to the long-suffering asthmatics themselves, but also to allow subsequent investigations of further new substances to proceed unhampered by erroneous and confusing estimates of the benefits of their immediate predecessors.

Reports from France and America on the clinical use of the new antihistamine substances (antergan, neonantergan, "benadryl," pyribenzamine) agree that good or even excellent results are obtained in the treatment of rhinitis, both seasonal and perennial; that markedly beneficial results follow the use of the drugs in various forms of urticaria and in some other dermatoses; that pruritus ani and vulvae and the pruritus of atopic dermatitis are often relieved and drug rashes benefited. Results in the treatment of asthma, however, are less certain.

Nevertheless enough has been published to encourage the belief that antihistamines do confer benefit in many cases of asthma, as Table I shows. From perusal of the American and French literature on antihistamines it is abundantly clear, however, that enough care has not always been taken to eliminate from the clinical trials those factors which contribute to erroneous clinical impressions. It is likely that herein lies the explanation of the otherwise irreconcilable variation in the apparent efficacy of these remedies in the hands of different workers.

TABLE I.—*A Selection of Results with Benadryl in the Hands of Different American Workers*

Author	Asthma (Seasonal)		Asthma (Perennial)	
	No. of Cases	No. Improved	No. of Cases	No. Improved
Levin (1946)	—	—	87	57
Waldbott (1946)	30	14	48	24
Koelsche, Prickman, and Carryer (1945)	19	14	12	4
Blumenthal and Rosenberg (1946)	—	—	12	4
McElin and Horton (1945) ..	—	—	3	1
Eyermann (1946)	—	—	4	3
Feinberg and Friedlaender (1946)	—	—	16	0

In most of the published reports on the antihistamines, especially in the treatment of asthma, clinical data are conspicuous by their absence. When authors write of their patients "deriving benefit," this statement is seldom amplified in any way, nor are the criteria of improvement indicated. In many cases the duration of the trial is not stated, nor, apparently, is the use of a control preparation thought to be necessary. These faults appear more plainly evident in those series in which the authors claim a high degree of improvement with antihistamines. To take a single instance, Levin (1946) reports the results of benadryl in the treatment of no fewer than 87 asthmatics, of whom as many as 67% of the children and 65% of the adults "obtained relief." Apart from stating that benefit was less in those patients who had a cold, the author gives no information at all about the patients; nor is this example an isolated instance.

The Present Investigation

In this investigation an attempt has been made to assess as accurately as possible the effect of one of the antihistamine preparations in asthma and hay-fever. In order to eliminate those factors which tend to create erroneous impressions, the patients have been very carefully selected and critically observed both while taking the trial preparation itself and while taking an inert dummy preparation of identical appearance. So that the criteria of success or failure with the trial preparation should not consist entirely of verbal descriptions of patients' subjective sensations, a system of numerical grading of the severity of the symptoms has been adopted, with the object of obtaining a graphic expression of the effect of the trial preparation itself as opposed to the effect of the control.

The compound used in this trial has been one of the newest and most active of the antihistamine substances—namely, pyranisamine maleate ("anthisan"), which is chemically N-dimethylaminoethyl - N - P-methoxybenzyl-α-amidopyridine acid maleate, otherwise called neoantergan maleate. It is a colourless crystalline solid, soluble in water. The preparation has been kindly supplied by Messrs. May and Baker put up in 0.1-g. tablets, coloured green, together with 0.1-g. tablets of identical appearance but composed of quite inert substances—namely, sucrose 50 g., lactose 350 g., starch 100 g.

Each patient has, unknown to him, received a quantity of the inert preparation alternating with the real substance. The initial dosage of both the inert and the real has been one tablet (0.1 g.) thrice daily. This has been increased to three tablets thrice daily after three days on the initial smaller dose. Patients suffering from nocturnal asthmatic attacks have also received 0.3 g. immediately before retiring at night.

The patients have been chosen from among those attending the Asthma Research Clinic at Guy's Hospital during 1946 and 1947. All have been under my direct observation.

Asthma Cases

The asthmatic patients comprised a mixed group of cases of different ages, sex, and duration, of various degrees of severity, with only one feature in common—namely, that all were examples of allergic as opposed to bronchitic asthma, with minimal infection and lung damage. However, although cases of primary bronchitic asthma were excluded from the trial, in the cases of very long standing there was bound to be emphysema and some degree of associated bronchial infection.

Twenty-five patients (12 male, 13 female) were included in the trial (Table II). Their ages ranged from 9 to 48 years. Most had perennial asthma, but some had seasonal exacerbations during June and July, over which period part of the trial was carried out. Of these patients 20 were well known at the clinic, and were particularly suitable for study, as either their asthma periodicity was regular or their symptoms were continually present. The remaining five were new patients with comparatively short histories, included in order to observe the effect of the preparation upon cases of recent onset. Cases 19 and 24 were excluded from the trial owing to the unexpected, startling, and sustained improvement that was produced by the inert control tablets.

The 20 patients had had a great deal of treatment both at Guy's and elsewhere. During the period of the trial it was not found practicable to withhold all other forms of treatment, and therefore, with the exception of the five new cases (Nos. 13, 21, 25, 26, 27), all the patients were instructed to continue with any palliative treatment to which they were

accustomed. The five new patients received the test substances only, and no other form of treatment. If they had been taking occasional ephedrine tablets these were withheld.

TABLE II.—*Asthma Cases*

Case No.	Age	Sex	Occupation	Duration of Symptoms
1	48	F	Housewife	40 years
2	48	F	,,	22 ,,
3	31	F	,,	12 ,,
4	30	F	,,	21 ,,
5	41	F	,,	18 ,,
6	28	M	Mechanic	6 ,,
7	37	M	Clerk	7 ,,
8	20	F	Housewife	17 ,,
9	19	F	Seamstress	2 ,,
10	27	M	Unemployed	2 ,,
11	33	M	Clerk	7 ,,
12	33	M	Fitter	1 year
13†	10	M	School	3 months
14	35	M	Clerk	30 years
15	29	F	Housewife	2 ,,
16	28	M	Independent	1 year
17	24	F	Typist	16 years
18	39	M	Clerk	2 ,,
19*	22	F	Journalist	4 ,,
20	41	F	Factory worker	5 ,,
21†	25	M	Clerk	9 months
22	31	M	Agent	2 years
23	11	M	School	6 months
24*	49	F	None	42 years
25†	18	F	Student	3 months
26†	9	M	School	8 ,,
27†	22	F	Typist	3 years

* Excluded from the trial. † Patients new to the clinic.

Hay-fever Cases

The hay-fever patients numbered 15 (Table III). All were skin-tested by the scratch technique and all were found to be sensitive to grass pollens. Cases 3, 9, and 14 were also sensitive to tree pollens. Four patients had asthma as well as hay-fever, but were not included in the asthma series as the unstable periodicity of their attacks made grading impossible. All the 15 cases had definite seasonal periodicity. Cases of perennial rhinitis were not included.

TABLE III.—*Hay-fever Cases*

Case No.	Age	Sex	Occupation	Pollen	Start of Symptoms	Start of Trial
1	21	F	None	Grass	June 1	June 8
2	24	M	Medical student	,,	May 29	,, 5
3	14	F	School	Grass and tree	June 4	,, 11
4	22	M	Medical student	Grass	May 20	,, 2
5	39	M	Storekeeper	,,	,, 25	,, 11
6	15	M	School	,,	June 2	,, 9
7	33	M	Traveller	,,	,, 11	,, 18
8	28	F	Housewife	,,	May 22	,, 5
9	21	M	Mechanic	Grass and tree	,, 14	May 21
10	27	M	Clerk	Grass	,, 16	,, 23
11	36	M	Farmer	,,	June 1	June 7
12	12	F	School	,,	,, 1	,, 7
13	34	F	Housewife	,,	May 18	May 25
14	32	M	Doctor	Grass and tree	June 14	June 21
15	40	M	Clerk	Grass	May 16	May 23

Scheme of Trial and Methods of Assessment

Asthma

Grading.—All the patients in the asthma group were graded according to the severity of their symptoms in the past (Table IV). The system adopted was similar to that recommended by the Asthma Research Council (Committee on Assessment of Results in Asthma). In the present series, however, an additional grade has been included, and it has also been found convenient to reverse the grading numbers, so that Grade 1 represents the mildest type of case instead of the most severe.

TABLE IV.—*Grading of Asthmatic Patients*

Present Series	Asthma Research Council	Symptoms
Grade 6	Grade I	Continual asthma. Patients who are unable to work at all or go to school
Grade 5	Grade II	Continual asthma. Patients who are able to work or go to school 75% of the time
Grade 4	—	Continual asthma. Patients able to work or go to school, but wheezy on at least one occasion during each 24 hours
Grade 3	Grade III	Patients whose attacks occur at least once a week
Grade 2	Grade IV	Patients whose attacks occur at least once a month
Grade 1	Grade V	Patients whose attacks occur less than once a month

Method.—The period of the trial for asthmatic patients extended over eight weeks, about half of which was spent on the active preparation, and the remainder, unknown to the patient, on the inert dummy tablets. For the first two weeks the dummies were used, after which the active preparation was substituted. After some weeks on the active preparation, patients returned to the dummies for a week or two before continuing with the active preparation. If a patient appeared to be showing a sustained improvement on the active preparation he was usually changed to the inert dummies.

At the start of the trial the patient was graded according to his past asthmatic history. At the end of each successive week of the trial he was regraded according to the severity of his symptoms during the preceding week. At the end of the eight-weeks period the average weekly grading number while taking the active preparation was available for comparison with the average weekly grading figure while taking the dummies. When the whole series of asthmatic patients had been investigated their average individual weekly grading numbers on the active preparation were added together for comparison with the sum total of the same figures whilst on the dummies (Table V).

TABLE V.—*Summary of Results in Asthma Cases*

Case No.	Grade Before Trial	Weekly Grade Nos.								Average Grade Nos. (Weekly)		
		1st	2nd	3rd	4th	5th	6th	7th	8th	U	D	R
1	6	6D	6D	6R	6R	6R	6R	6D	6R	6	6	6
2	5	5D	5D	4R	3R	3D	5R	5D	5R	5	4·5	4·2
3	5	5D	5D	5R	5R	5D	5R	5D	5R	5	5	5
4	6	6D	6R	6D	6R	—	—	—	—	6	6	6
5	5	5D	5D	4R	5R	4D	5R	4R	5R	5	4·6	4·5
6	3	3D	3D	4R	2R	3R	4R	3D	3R	3	3	3·2
7	4	4D	4D	4R	4R	5R	5R	—	—	4	4	4·5
8	3	2D	2D	2R	2R	2R	2R	3R	3R	3	2	2·3
9	3	3D	3D	3R	3R	3R	3D	3D	3R	3	3	3
10	4	4D	4D	3R	3R	4R	4D	4D	3R	4	4	3·2
11	5	4D	4D	4R	3R	3R	2R	2D	4R	5	3·3	3·2
12	5	4D	3D	3R	4D	4D	3R	4R	4R	5	3·7	3·5
13	4	4R	4R	4D	3D	3R	3D	3D	4R	4	3·2	3·7
14	4	4D	4D	3R	3R	4D	3R	3R	4D	4	4	3
15	3	3D	3D	3R	3R	3R	3D	2D	2R	3	2·7	2·7
16	3	3D	3D	3R	3R	3R	3R	3D	3D	3	3	3
17	3	3D	3D	3R	2R	3R	3D	3D	3R	3	3	2·7
18	3	3D	3D	4R	3R	2R	3D	3D	3R	3	3	3
19*	4	3D	2D	2D	2D	2D	4U	4U	2D	4	2·1	—
20	3	3D	2D	2R	2R	3R	3D	2D	2R	3	2·5	2·2
21	4	4R	4R	3D	3D	3D	4D	3R	3R	4	3·2	3·5
22	3	4D	3D	3R	2R	3R	3R	3D	3D	3	3·2	2·7
23	4	3D	3D	3R	3R	3R	3R	3D	3D	3	3	3
24*	4	3D	2D	2D	3U	3D	2D	4U	3D	3·5	2·5	—
25	4	3D	2D	2R	4R	3R	3D	4D	3R	4	3	3
26	4	3D	3D	3R	4R	3R	4D	3R	3D	4	3·2	3·2
27	4	4D	3R	2R	3R	4D	3R	3R	4D	4	4	2·8
Total grade nos. for whole series										99·0	90·1	87·1
Average weekly grade nos. for whole series										4	3·6	3·5

* Not included in trial. U = Untreated. D = Dummy. R = Real.

It is not intended that any statistical significance should be attached to these figures. The grading numbers serve as convenient numerical symbols representative of the degree of severity of the asthma of each patient week by week. The figures, however, do bear a definite fixed relation to the severity of the symptoms, so that the sum total of the average weekly grading numbers for the whole group on the real, as opposed to the inert, preparation may be taken as a reflection of the summation of the severity of the asthma of all the 25 patients while taking neoantergan, compared with the severity of their symptoms while they were not.

Hay-fever

Grading.—The symptoms of hay-fever patients have been divided into four grades according to the severity—i.e., Grade 4, severe symptoms; Grade 3, moderate symptoms; Grade 2, slight symptoms; Grade 1, no symptoms.

Method.—A scheme similar to that used for the asthma patients has been devised for the hay-fever patients. Owing to the comparatively short duration of the symptoms in some

cases the period of time on the dummy tablets has been curtailed to a week in most instances, while that on the active preparation has ranged from four to seven weeks. The results are shown in Table VI.

TABLE VI.—*Summary of Results in Hay-fever Cases*

Case No.	Weekly Grade Nos. Results	Average Weekly Grade Nos. Untreated (u)	Dummy (d)	Real (r)
1	4u4d2r2r2r1r	4	4	1·8
2	4u4d3r2r1r2r1r ..	4	4	1·8
3	4u4d3r1r2r2r	4	4	2
4	3u3d2r1r3d1r1r1r ..	3	3	1·2
5	4u4d1r4d1r1r1r.. ..	4	4	1
6	4u4d3r2r1r1r1r1r1r ..	4	4	1·4
7	4u4d1r1r1r	4	4	1
8	4u2r3d2r	4	3	2
9	4u4d1r1r4d1r1r1r ..	4	4	1
10	4u4d3r3r2r2r2r ..	4	4	2·4
11	4u4d1r2r1r1r1r ..	4	4	1·2
12	3u3d2r2r3d1r1r ..	3	3	1·5
13	4u4d2r2r4d2r2r2r ..	4	4	2
14	3u1r1r3d1r	3	3	1
15	4u4d3r2r4d2r2r2r2r ..	4	4	2·2
	Total	57	56	23·5
	Average for series ..	3·8	3·73	1·5

Discussion

Before this investigation began a few cases of asthma and hay-fever had been treated with neoantergan, with apparently extremely disappointing results in the former and very encouraging results in the latter condition. The tentative impression of the powers of this drug thus created has been confirmed in striking manner by the more detailed observations on the series of cases summarized above.

In the asthmatic group the average of the weekly grading figures for the 25 patients observed over 105 weeks while taking neoantergan was 3.5. The equivalent figure for the same 25 patients observed for 89 weeks on the control tablets was 3.6, and before treatment was started the figure was 4. In other words, there appeared to be no appreciable difference in the severity of the symptoms while taking the drug, as opposed to the control tablets.

In contrast to the asthmatics, the severity of the symptoms of the 15 hay-fever patients while taking the preparation over a period of 69 weeks was indicated by the figure 1.5, whereas the severity of the symptoms of these patients observed over 21 weeks on the controls was indicated by the figure 3.7—a very striking contrast indeed.

These graphic expressions of results strongly reinforce the clinical impression of the benefit of the drug in this series—namely, that in asthma neoantergan appears to be of little or no value, whereas in hay-fever the symptoms have been partially or completely controlled in all the patients who were taking the preparation, including a number with severe symptoms.

The necessity for using a control preparation in an investigation of this kind is illustrated by asthma cases Nos. 19 and 24. Both these patients showed a great improvement in their asthma as soon as they began to take the dummy tablets, and not only was the improvement sustained throughout the period of the trial but both patients became worse when the dummy tablets were withheld. Case 24 was of particular interest, as this patient had previously been a severe asthmatic in Grade 4—a case of very many years' standing—and was also suffering from atopic dermatitis, which, however, remained unaltered in spite of the improvement in the asthma.

Even before this trial it was considered improbable that neoantergan would prove capable of influencing materially the severe asthmatics of Grades 5 and 6. It was to be hoped, however, that some of the patients with milder degrees of asthma might show some improvement—for example, those with only a moderate degree of daily or nocturnal wheeziness or those who suffered from one or two mild attacks of short duration weekly. The published reports of other workers led me to expect some improvement in patients of this kind, but none was forthcoming which could with justification be ascribed to neoantergan; in fact, improvement in Grades 3 and 4 appeared just as likely to occur with the control as with the real preparation, and in any event was usually fluctuant and variable. For example, asthma patient No. 2, a severe case, had two good weeks as soon as she went on to the real preparation; but this improvement persisted even when the control was substituted, and when she finally did relapse the previous degree of improvement could not again be achieved with the active preparation.

It did not seem that a short duration of the patient's history favourably influenced the results with neoantergan. Asthma cases Nos. 13, 21, 23, 25, and 26 had all had asthma for less than a year, but none showed any improvement—in fact, Cases 13 and 21 actually appeared to be worse during treatment. Neither did the youth of this particular group of patients impart any salutary effect.

In spite of its soporific effect neoantergan conferred no apparent benefit upon patients whose asthma showed a nocturnal periodicity. For example, asthma case No. 7, a young clerk, had an attack every night with clockwork regularity, usually at about 3 to 4 a.m. This had persisted even during treatment as an in-patient, and sleeping by day instead of by night made no difference, the asthma again occurring some five hours after retiring to rest. This man received a large dose of neoantergan as a preventive immediately before getting into bed, but the attacks occurred just the same. Nor did the drug appear to exert any appreciable effect in relieving the established attack, which, however, invariably responded to adrenaline. It was of particular interest to note that after the trial was over Cases 16, 18, 20, 21, and 26 improved at once on adrenaline, which they had not previously taken, except occasionally. The improvement was sufficient to move Cases 21 and 26 down a grade as soon as they had mastered the technique of self-injection of adrenaline.

In addition to the object-lesson of Cases 19 and 24, both of whom did so well on the inert control tablets, another point of interest emerges from the grading results—namely, that the patients' grading figures (3.6) during the trial while taking the dummies were considerably lower than the figures (4) for the same cases before the trial, in spite of careful assessment of the grades based on previous observation of the individual patients over periods of time ranging from several months to several years. It is easy to see how, if a control preparation had not been used, such a change in symptoms could be mistaken for an improvement due to the test drug.

There can be no doubt at all of the value of neoantergan in the symptomatic treatment of hay-fever. In addition to the striking changes in the grading figures while taking the preparation (1.5) compared with the figures on the dummies (3.7), the patients themselves were unanimous in their praise of the preparation, although disappointed during periods on the dummy tablets. Some of these patients had had pollen-desensitization courses in the past, several of them more than once. They declared that neoantergan conferred as much protection as any but the most successful desensitization course. Two patients, not included in the trial, were treated with a high degree of success with neoantergan, which was started half-way through the season when their pre-seasonal desensitization course was found to be not wholly effective.

Side-effects.—Of the 42 patients reported in this trial side-effects were noted in 23—10 had slight nausea, 6 nausea and drowsiness, 4 drowsiness, 1 impotence, and 2 giddiness.

Conclusions

Neoantergan conferred no apparent benefit upon 25 specially selected and carefully observed asthmatic patients.

Neoantergan was markedly successful in reducing the severity of the symptoms of 15 cases of hay-fever.

When working with asthmatic patients an erroneous impression of the efficacy of a new preparation is likely to be formed unless a very careful scheme of trial is planned, preferably using a control preparation.

It is with pleasure that I acknowledge the help received from Dr. W. N. Mann during this investigation, and I am grateful to Dr. W. R. Thrower, of Messrs. May and Baker, for kindly supplying the anthisan. This work is an abstract from part of a Cambridge M.D. thesis, and for permission to publish it I am indebted to Sir Lionel Whitby, Regius Professor of Physic, Cambridge University.

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CHIASMA LESION DUE TO FALL IN EPILEPTIC FIT

BY

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AND

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Damage to the optic nerve due to a fall in an epileptic fit is surprisingly rare, although optic-nerve lesions may follow slight head injuries. Chiasmal damage occurring after epileptic seizures has not been previously recorded in the literature. The following case, which ended in optic atrophy and blindness in one eye, is of special interest because of its unusual course and visual-field changes.

Case Report

The patient, a single man aged 32, suffered from epilepsy, probably of traumatic origin. Generalized fits followed a severe head injury sustained six years before. These recurred at intervals of one to two months, with sudden falls and no aura. At the end of November, 1944, he fell on his forehead during a fit. There was a swelling over the right eye due to extravasation of blood. He was confused for the rest of the day—as usual after his seizures. Next day, when mentally clear, he complained of blindness in his right eye. Examination revealed a complete loss of vision in this eye, and a marked temporal-field defect of the left eye with normal visual acuity. This was evident in subsequent examinations. Simple and stereoscopic *x*-ray examination of the skull immediately afterwards did not show any fracture.

About a fortnight after the accident there was a distinct difference in the two disks, the right being paler. After a month there was an obvious atrophy of the right disk, with paleness, narrowing of the large retinal arteries, and reduction of the small vessels. This condition was still unchanged when a complete examination of fundus, visual field, and acuity was carried out in May, 1945, six months after the accident. Since further developments were not anticipated no regular examinations were made. On July 17, 1945, however, the patient reported that a few days previously he had begun to see again with the right eye and that vision had gradually improved. Immediate examination showed a central scotoma in his right eye with full peripheral visual fields. The visual acuity for finger-counting was 3 ft. (0.91 metre). An examination two days later showed that the central scotoma had disappeared and that the acuity had risen to 6/9. The visual field in the left eye still showed some temporal defect, but to a less degree than in the first period after the accident.

On Aug. 2 he reported that the sight of the right eye had again become worse, and attributed this to an injury inflicted by a patient, who he alleged threw lumps of soil into his face. He also stated that a few days previously he had had to bend his head while helping with weeding in the garden. The visual field two days later showed a central scotoma and a concentric constriction of the peripheral field; the visual acuity had fallen to 1/60. Subsequent examinations showed that the scotoma gradually increased in size, the peripheral field became more and more restricted, leaving eventually a pericentral annular island of vision, and within a week the patient was again blind in the right eye. The visual field of the left eye showed no definite temporal defect during this phase. The direct pupillary reaction to light in the right eye was from the beginning of the observation sluggish and poor, decreasing in the first week after the accident until it became fairly stable after the atrophy of the optic nerve had been established. No definite change was noted during the short spell of recovery. Up to January, 1948, no further change has occurred; the right eye remains blind, with atrophy of the disk; the left eye shows full visual field and normal acuity. The direct light reaction, though very poor, is still obtainable.

Discussion

Complete blindness and optic atrophy of the right eye after a fall in an epileptic fit, and a temporal-field defect of the left eye, pointed to a lesion in the chiasmal region affecting the fibres of the right optic nerve and the nasal retinal fibres from the left eye. This type of injury has been repeatedly discussed in the literature. The skull fracture which often accompanied such lesions suggested a direct traumatic damage to the nerve, and specimens have been shown in which the nerve in this section had actually been torn. Early writers were mainly concerned with the possible types of skull injury which might produce this nerve damage. Various mechanisms have been suggested (Liebrecht, 1912; Coppez, 1929; Rand, 1937), but more recent experience has made it clear that bone injury and anatomical nerve lesions are not the only cause of the traumatic chiasma syndrome, and that vessel damage alone may have the same effect and produce the initial symptoms (Traquair, 1933, 1942; Dandy, 1932; Rodger, 1943; Hughes, 1943). Rodger differentiates bleeding into the sheaths and subvaginal and intraneural haemorrhages.

There can be little doubt that in our patient there was a vascular lesion; the remission and subsequent relapse cannot be explained in any other way. The fact that central vision was the last to return when the recovery took place, and that a central scotoma was the first symptom when the relapse occurred, seems to indicate an intraneural damage. The onset immediately after the injury is in favour of traumatic rupture of the vessel wall, with consequent intraneural haemorrhage (Rodger, 1943). This would also account for the relapse. After a slight injury the vessel, which had been closed, started to leak again, causing a gradually increasing extravasation—a mechanism well recognized in meningeal and brain-vessel damage, when a minor incident may cause renewed extravasation long after the initial trauma.

With regard to the progress of our case the changes during the first few weeks after injury were as anticipated. It is the general experience that a visual-field defect and loss of visual acuity occur immediately after the injury, while atrophy of the optic nerve usually appears within four weeks. In seven cases of optic-nerve lesions Rodger (1943) noted an average interval of 17 days, the shorte-

interval being four days. In our case blindness set in immediately after the accident, and atrophy was distinct after a fortnight.

Concerning the prognosis of these cases there has been general agreement (Traquair) that if no signs of improvement in visual acuity occur during the first four weeks no further change can be expected. But in our patient there was a rapid and almost complete recovery as late as five months after the injury. This is difficult to explain; it is contrary to all experience that recovery should have started after so long a time. One might think of a hysterical fixation of an original organic blindness, but nothing was observed in the general behaviour of the patient to support this, and there were no psychogenic elements. There were, on the other hand, optic atrophy and a transitory scotoma—findings which do not permit a functional explanation.

It is likely that the primary site of the lesion was in or near the anterior chiasmal angle, affecting mainly the right optic nerve but also damaging the crossed fibres of the left. It is interesting to note that the temporal-field defect of the left eye gradually diminished and had entirely disappeared after the relapse. We will therefore have to assume that on this occasion the chiasma had been spared, the lesion being restricted to the right optic nerve.

Summary

A case is reported in which blindness and optic atrophy in the right eye, with a temporal-field defect in the left eye, followed a fall in an epileptic fit. *X*-ray examinations of the skull were negative. There was no fracture.

Not less than five months after the injury normal visual acuity with full visual fields in the left eye were re-established; during this period of recovery central vision was the last to return to normal. The temporal-field defect in the left eye was at the same time greatly reduced.

Shortly afterwards, following a trivial blow on the face, his sight and visual-field condition deteriorated, a gradually extending central scotoma appeared, and visual acuity fell rapidly until the right eye became blind again. There was no temporal-field defect in the left eye at this time. Atrophy of the right disk remained unchanged during the whole period. There was no further change one year later.

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Dr. Esmond R. Long, director of medical research and therapy, National Tuberculosis Association, has been appointed editor-in-chief of the *American Review of Tuberculosis*, official journal of the N.T.A.'s medical section, the American Trudeau Society, to succeed the late Dr. Max Pinner. A new position of managing editor has been created, and Dr. Walsh McDermott, associate professor of medicine, Cornell University Medical School, New York, has been appointed to the post. Dr. Long, who is also director of the Henry Phipps Institute, Philadelphia, has been director of the N.T.A.'s medical research since January, 1947. He is a past president of the N.T.A. and is a consultant on tuberculosis to the United States Army, the Veterans Administration, and the U.S. Public Health Service. A graduate of the College of Physicians and Surgeons, Columbia University, Dr. McDermott is associate attending physician of New York Hospital and was associate editor of the seventh and eighth editions of the Cecil-Loeb *Textbook of Medicine*. He is a member of the American Trudeau Society's Committee on Medical Research and Therapy and of the Antibiotics Study Section and the Tuberculosis Study Section, National Institute of Health, U.S. Public Health Service.

JUVENILE GENERAL PARALYSIS

A CASE WITH A SPONTANEOUS BUT SHORT-LIVED REMISSION

BY

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Although a considerable number of cases of juvenile general paralysis have been reported in the literature the disease is relatively rare and its incidence in cases of congenital syphilis is stated by Stewart (1933) to be about 1%. Schmidt-Kraepelin (1920) gives the figure as 1.7%, but White and Veeder (1922) and Smith (1933) are in agreement that the incidence is less than 1%. Most authorities agree that the sex distribution is approximately equal, although there is a slight tendency towards a preponderance of males; thus out of 145 cases reported by Mott (1899), Watson (1903), Schlicht (1915), Schmidt-Kraepelin (1920), Klauder and Solomon (1933), and Menninger (1930), 83 were males and 72 females. According to Menninger (1936) there are two types of onset, the first being insidious, when the child is apparently subnormal from birth, and the second in which an acute breakdown occurs after several years of seemingly normal development. Menninger in an analysis of 542 cases gives the age of onset as 3 to 5 years in 9.4%, 6 to 10 years in 24%, 11 to 15 years in 36.2%, 16 to 20 years in 26.8%, and 21 to 25 years in 3.6%. In the majority of cases, therefore, the illness begins between the ages of 10 and 15. Menninger states that in a series of 653 cases psychic trauma was regarded as the precipitating factor in 2.7% and that convulsions occurred in 17% before the diagnosis was established.

Case Report

A boy, aged 11 years 3 months, was admitted to this hospital in November, 1946, as he was not responding to outpatient treatment at a child-guidance clinic in another area.

Family History.—The *father*, a Naval petty officer aged 38, was stated to be fit and well. He has had little to do with the boy's upbringing owing to his service overseas. When interviewed in December, 1946, he admitted that he had had primary syphilis in 1929 but had received a full course of treatment over two years. His Wassermann reaction was: blood +, C.S.F. negative. He was having treatment at a V.D. clinic. The *mother*, aged 36, is fit and well. She is a kindly woman, but ineffective in handling the family and lacking in understanding. Her Wassermann reaction was: blood +, C.S.F. negative. She has had no treatment. *Siblings:* There are three sisters, aged 16, 7, and 4. All are bright and alert, with negative serology.

Personal History

The boy weighed 8 lb. 12 oz. (3.98 kg.) at birth, walked at 12 months, and began talking at 15 months. Clean habits were established early, and he appears to have been a perfectly normal child until a few days before his fifth birthday, when his home was destroyed by enemy action. He was uninjured, but was said to have screamed persistently for several hours after the incident. He was apparently terrified during the next three days, and there were many outbursts of screaming during this time. On the fourth day he had an epileptiform attack during which he exhibited loss of consciousness and left-sided rigidity followed by generalized clonic movements. In the succeeding nine months he had frank epileptic major attacks with incontinence and tongue-biting at the rate of about one a week. These persisted despite anticonvulsant drugs prescribed by his doctor. During this time he progressively became more dull and was excessively timid and anxious. There was, in fact, a complete personality change, and whereas he had formerly been a bright, cheerful, alert, self-possessed child, he now became very quiet and reserved, and was made fun

of by other children. Six months after the original epileptic manifestation he was seen by a children's psychiatrist, who stated that he was suffering from an anxiety state but that no special treatment was required. Shortly before this it had been noticed that he was becoming very clumsy and had very great difficulty in picking up objects. It was also noted that he had to be assisted in dressing, as he was unable to do up his buttons or tie his shoe-laces. His speech, which had previously been quite clear, became slurred, and his parents and teachers had difficulty in understanding what he was trying to say.

In July, 1942, the family moved to Scotland, and shortly after this a remarkable change was noted in the child. In the course of a few months he completely lost all signs of muscular incoordination, his speech became clear, he regained confidence, and he began to stand up for himself with other boys. He rapidly made progress in education, and during the next two years became recognized as one of the best scholars in his year. Evidence of this exists in the fact that he was awarded several books as prizes in arithmetic, writing, spelling, and drawing. In September, 1944, the family moved to another area and very shortly John's condition began to deteriorate once more. His standard at school fell rapidly, but his mother attributed this to the change of school. By February, 1945, however, it became obvious to his parents that his symptoms were exactly similar to those noted at the age of 5. A school report in May, 1945, noted him as "dull and backward" but "very nervous." He was accordingly referred to a child-guidance clinic and was treated as a "maladjusted child." His I.Q. was reported as 100. It is of interest to note that his mother had observed that his drawings were becoming completely indecipherable, being entirely obscured by a wealth of unnecessary detail. As three months' treatment did not make any impression on the child, but on the contrary had failed to prevent deterioration, he was sent to this hospital for in-patient treatment.

On examination he was a plump, awkward-looking child who was very restless and apprehensive. It was noted that the incisors were of the Hutchinsonian type. Gross motor incoordination was present, and this rendered him ludicrously clumsy. Slurring of articulation was a prominent feature, and although the pupillary responses were fairly normal there was irregularity of the margins. Tongue tremor was present and all reflexes were exaggerated; plantar responses were flexor. He was dull, slow in comprehension, and his I.Q. was found to be 69. The diagnosis of juvenile paresis was confirmed by a triple positive Wassermann reaction in both blood and cerebrospinal fluid and a paretic gold curve in the Lange test.

Since admission his condition has continued to deteriorate despite treatment, and he now falls about, has numerous epileptiform attacks, is incontinent, and requires constant nursing care and supervision.

Discussion

The above history has been carefully checked by reference to practitioners who previously treated the child, to teachers, and to others. It will be noted that the onset was just before the age of 5. So far as can be ascertained there are only 14 cases recorded in the literature in which the age at onset was the fifth year. Spontaneous remission is indeed very rare, and Stewart (1933) states that "the disease is never interrupted by a remission." On the other hand, Alzheimer (1895), Thompson and Dawson (1895), and others have recorded instances of spontaneous remissions, but the total number of cases does not exceed 20. Most authorities agree that the prognosis in such cases is very poor, and Lurie *et al.* (1943) report on 8 cases of juvenile paresis seen at the Cincinnati Child Guidance Home. Despite early diagnosis and treatment all these children showed progressive mental and intellectual deterioration.

The fact that this boy was examined by two child psychiatrists and treated by one for three months should make plain the need for a careful physical examination of all children seen at child-guidance clinics. In this connexion it is of interest to note that out of 125 in-patient children reported by Barker and Milligan (1947) 13 were found to be suffering from organic disease of the nervous system and only three of these cases had been diagnosed as such before admission to hospital.

Summary

A case of juvenile general paralysis is described, with an onset at the age of 5 and an apparently complete spontaneous remission of two years' duration.

I wish to thank Dr. Thomas Beaton, Physician-Superintendent, St. James Hospital, Portsmouth, for permission to publish this case record.

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Medical Memoranda

Gastric Herpes Zoster

The following report of a case of haematemesis due to gastric herpes zoster is worthy of record.

CASE HISTORY

A diabetic woman aged 66 was admitted in a precomatose condition with a blood sugar of 450 mg. per 100 ml. She had been under regular observation in the diabetic clinic, and had no history of gastric symptoms. One year previously she had fallen and bruised her left lower ribs, and since that time she had noticed intermittent vague pain in the same region. A week before admission this had become constant and more severe, radiating round to the left abdomen. Four days later, feeling ill, she remained in bed, and at noon had a sharp haematemesis. At 3 p.m. she noticed a rash on the abdomen to the left of the umbilicus. On account of her malaise she discontinued both food and insulin; her diabetic precoma was the direct result.

On examination, apart from the signs of dehydration, she showed slight central epigastric tenderness. A typical eruption of herpes zoster was present on the left chest and abdomen, apparently involving thoracic segments 9 and 10. The rest of the examination was normal. Her diabetic condition was successfully treated, but unfortunately it was severe enough to preclude gastroscopy. A barium meal x-ray film eight days later was normal, and a fractional test meal showed complete achlorhydria. Haemoglobin was 90%, and rose subsequently with treatment. A radiograph of the spine and ribs was normal. The cerebrospinal fluid on admission contained 70 mg. of protein per 100 ml. and 23 lymphocytes per c.mm. Nine days later the protein was 50 mg. and there were 10 lymphocytes.

COMMENT

The sympathetic supply of the stomach by way of the coeliac plexus almost certainly includes branches from the ninth and tenth thoracic nerves. The appearance of the somatic eruption within three hours of the haematemesis is very suggestive of a true gastric herpes zoster as the origin of the latter. The relation of the previous injury to the herpes is of interest. Although there was no evidence of bony injury, it is possible that the repeated painful stimuli from an organized haematoma in muscle may have been sufficient to render the affected segments liable to attack by the virus. The cerebrospinal fluid changes are typical of those found in herpes zoster.

I wish to thank Prof. T. H. Oliver for permission to describe this case.

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Reviews

KEEPING FIT

Physical Fitness Appraisal and Guidance. By Thomas Kirk Cureton, Jr., M.A., M.P.E., Ph.D., assisted by Frederick W. Kasch, B.S., M.S., John Brown, B.S., and W. G. Moss, M.S., Ph.D. (Pp. 566; illustrated. 30s.) London: Henry Kimpton. 1947.

What does physical fitness mean? This, the opening sentence of this remarkably comprehensive work, prompts the supplementary inquiry, Fit for what? In the past, attention has been particularly, indeed almost exclusively, directed to the circulation as the limiting factor in physical endurance. It is clear that specific tests must be instituted to assess capability for a particular purpose; for emotional, mental, and social fitness are also important in adaptation to life and living—problems which, the author indicates, will be investigated in future. As we must repeat *ad libitum*, perhaps *ad nauseam*, it is to the U.S.A. that we look for research in this subject. Interest and opportunities there permit grand-scale organization and operations with unlimited subjects for investigation, luxurious equipment, and staff to conduct the investigation. All of these are reflected in the present work—a stupendous compilation of details, page after page of charts and graphs and columns recording the results of tests of physical fitness and physique ratings.

What are the conclusions? To a great extent only an elaboration of the obvious, a reminder of what is already known, a repetition of the opinions expressed by workers in all parts of the world. We see, however, the beginning of an important study of "body types." "Just as we can purchase 10 dollar suits or 100 dollar suits, so some of us inherit 10 dollar organs and others 100 dollar organs." How far can we estimate virility and longevity on the basis of certain constitutional body types? We see in this work's subtitle the claim that "appraisal" permits of "guidance" to utilize natural advantages to the utmost, to accept the limitations imposed by natural deficiencies and so avoid disappointments in attempting to achieve the impossible.

The student of athletics will look for references to the super performer. In a chapter entitled "Analysis and Prediction of All-out Athletic Performance" the author speculates on the factors governing the quality of great endurance. He quotes (from *Cardiologia*, 1945, 9, 313) Gustav Nylin's investigation on the blood circulation of Gunder Hägg and Arne Andersson, the great Swedish middle-distance runners who broke several world records. It is interesting to learn that the most elaborate observations could only confirm the clinical examination which was made when these athletes visited Britain two years ago in the conclusion that no specific explanation was forthcoming of their remarkable performances. It is simply a matter of superior co-ordination of all the factors concerned in violent exercise.

The authors include a table of the "calorie value" of all forms of physical exertion from knitting to sprinting at full speed, which underlines once more the popular misconception that obesity can be treated by exercise. Doubtless exercise contributes to its reduction so long as dietetic restrictions are simultaneously imposed. The fat man will be dismayed to learn that in order to work off a pound of fat it is necessary to walk 66½ miles at the rate of 3½ miles an hour, which is a fairly strenuous pace for the average person of sedentary habits. or to run at full speed (10 yards per second) for 7½ miles, were this humanly possible.

ADOLPHE ABRAHAMS.

PRACTICAL BIOCHEMISTRY

Laboratory Instructions in Biochemistry. By Israel S. Kleiner, Ph.D., and Louis B. Dotti, Ph.D. Second edition. (Pp. 245. 12s. 6d.) London: Henry Kimpton. 1946.

This manual of practical biochemistry is primarily intended for medical students. The selection of material and the standard of instruction are good, being based upon several years of practical experience in New York Medical College. The book compares favourably with manuals used by medical schools in this country which for some inexplicable reason rarely seem to reach the publisher's office. The authors cover the basic requirements of clinical chemistry well, and as an innovation include accounts of such estimations as acid and alkaline phosphatase, cholesterol-ester ratio, and Bratton-Marshall's method for sulphonamides. There is a new section on analysis of cerebrospinal fluid, and a courageous attempt has been made to introduce the student to blood-gas analysis. With the development of the technique of heart catheterization such analysis will become of considerable clinical importance.

The book suffers from the disadvantage of all practical manuals in that, divorced as it is from its theoretical background, it lacks continuity with the course in organic chemistry which should precede it and the course of clinical chemistry which should follow. A practical account of a simple metabolic investigation is welcome; it is a feature which might with advantage have been extended to cover a few simple clinical tests. Students in Britain will find it difficult to carry out the instructions on experimental diets. The quality of the paper, which for the most part is printed on one side only, is first class. A novel plastic binding allows individual pages to be removed and gives the book an attractive appearance; nevertheless, it is unlikely that it will survive even normal use for more than a few years, and a more orthodox and permanent binding would have been preferable.

A. E. KELLIE.

A PHYSICIAN'S PHILOSOPHY

The Philosophy of a Scientist. By R. G. Gordon, M.D., D.Sc., F.R.C.P.Ed. (Pp. 206. 16s.) London: Hutchinson's Scientific and Technical Publications. 1948.

The contributions of members of our profession to philosophy, in all senses of that word, have been illustrious. Speaking of Locke, Dugald Stewart wrote:

"No science could have been chosen, more happily calculated than Medicine, to prepare such a mind for the prosecution of those speculations which have immortalized his name; the complicated and fugitive and often equivocal phenomena of disease, requiring in the observer a far greater proportion of discriminating sagacity than those of Physics, strictly so called; resembling, in this respect, much more nearly, the phenomena about which Metaphysics, Ethics and Politics are conversant."

Some readers of Dr. Gordon's thoughtful treatise may think that he quotes over-abundantly, and a reviewer certainly should eschew quotations, but the following passage illustrates happily what Dugald Stewart had in mind:

"There are some people who think so little, that their sole philosophy is to do as their neighbours do and conform to the customs of the tribe, whether that tribe be a community of primitive savages or a social set in a provincial town. This may work well enough so long as things go on relatively smoothly and the tribe remains a coherent body, but if some upheaval occurs, whether in the personal life of the individual or in national politics, which flings them out of their envelope of protective custom, these people may become very lost and very distressed. They are apt to suffer from one variety of what is popularly called a nervous breakdown. This may cause them the more distress in as much as, previously, they have thoughtlessly adopted the attitude of insolent superiority, bred of ignorance and prejudice, with which their set have regarded those suffering from something which they do not understand. To find that they themselves are afflicted with such a complaint fills them with such shame that they insist that they must be suffering from some organic disease, which in their eyes is much more respectable and for which they would expect full sympathy, which they would never dream of extending to their miserable neurotic brethren."

Perhaps that admirable passage may attract colleagues to whom the word philosophy is as repellent as the word ideology to the reviewer. Dr. Gordon's philosophy, like that of Horace, is:

> Aeque pauperibus prodest, locupletibus aeque,
> Aeque neglectum pueris senibusque nocebit.

It appertains to what in the eighteenth century would have been classed as natural theology, but Dr. Gordon's knowledge of twentieth-century science is more exact than the knowledge eighteenth-century deists had of Newtonian mathematical

physics. Dr. Gordon sets out fully the difficulties which a consistent philosophy of the universe, or theology, must reconcile and insists that each man must face those difficulties for himself; he may end by reaching conclusions long ago propounded, but they must be his conclusions. As the first Marquis of Halifax said, "Men who borrow their opinions can never repay their debts." It is not a sneer but a psychological truth that each man must make his own God; yet the result may not differ superficially from the God of a "revelation." It differs, however, fundamentally in as much as it is realized by the individual. Dr. Gordon's holistic conception of the soul and Aristotle's entelechy do not seem very different, but the two philosophers have travelled by different routes.

Dr. Gordon's philosophy is optimistic. He believes in ethical progress and reminds us that, on a cosmic time scale, civilization is young. Perhaps one needs more than an average degree of altruism to be comforted by his argument, but certainly an honest student will learn from Dr. Gordon's book some useful lessons in self-discipline.

MAJOR GREENWOOD.

GROWTH OF A VOLUNTARY HOSPITAL

The Story of a Scottish Voluntary Hospital. The Royal Northern Infirmary, Inverness. By T. C. Mackenzie, M.D., F.R.C.P.Ed. (Pp. 279. 8s. 6d.) Inverness: The "Northern Chronicle" Office.

The author of this interesting study of the inception and growth of a typical Scottish voluntary hospital presents a panorama in miniature of the changing social standards and advances in medical practice during the past 150 years against a background of the detailed administration and inevitable development of a living institution meeting an increasing need. Conceived in 1797 as a means of affording effectual aid to the sick poor in the Highlands of Scotland, and nurtured through the years by the generosity and devotion of succeeding generations of public-spirited individuals, the Inverness Infirmary has grown from small beginnings into the Royal Northern Infirmary, the acknowledged medical centre for the Northern Region of Scotland. The author has compiled the story from contemporary records and reports, and excerpts from the minutes of the Weekly Meetings of Committee give colour and human interest to the recurring pattern of increasing demands having to be met by increasing expansion and greater efforts to enlarge the funds. From the earliest days the interest of the managers and staff in the detailed administration of the hospital is clear—even concern about the vagaries of the Infirmary cow is recorded—as well as their interest in the welfare and progress of the patients.

To the student of medical and social history interesting glimpses are afforded of the values, human and monetary, accepted in the early part of last century. It is startling to realize that the provision for the "lunatick poor" consisted of cells—8 feet square—and that in 1811 one of the staff reported to the Committee that a female lunatic who had been in the Asylum for nearly 12 months "was so far recovered, that she might be allowed to leave her cell with safety, but as she was quite destitute of cloaths—being literally in a state of perfect nudity—the doctor suggested the propriety of furnishing her with some." Fifty years before Florence Nightingale the nurse ranked with the cook and chambermaid, with a wage of £4 yearly, and the matron's wage at £10 was less than the gardener's.

This book throughout illustrates clearly the gradual evolution of the voluntary hospital, which through the initiative and enterprise of private individuals has constantly been in advance of public authorities in meeting the needs of the community. As the author states in his preface, the knowledge of such a history is of special interest and importance at the present time, when the trend of events points to the assumption by the Government of departmental and possibly bureaucratic direction and control in the sphere of hospital work. Dr. Mackenzie has shown "a sound judgment and a mature understanding" in his compilation, and his hope that many readers who think kindly of the North may find much of interest in this book should be entirely fulfilled.

E. A. CORMACK.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

Males and Females. By R. Pilkington. (Pp. 92. 6s.) London: Delisle. 1948.

An introduction to the physiology of sex for adolescents.

Education and Health of the Partially Seeing Child. By W. Hathaway. 1st ed. Revised. (Pp. 216. 14s.) London: Geoffrey Cumberlege. 1947.

Intended for teachers, administrators, and nurses.

Congenital Malformations. By D. P. Murphy, M.D., F.A.C.S. 2nd ed. (Pp. 127. 30s.) London: J. B. Lippincott. 1947.

A practical introductory account of the causes of congenital malformations.

Diagnosis in Daily Practice. By B. V. White, M.D., and C. F. Geschickter, M.D. (Pp. 693. £4 10s.) London: J. B. Lippincott. 1947.

A textbook of diagnosis intended for the general practitioner and house-man.

Restoration Exercises for Women. By E. Rout. Preface by Sir Arthur Keith, F.R.S. 9th ed. (Pp. 84. 7s. 6d.) London: William Heinemann. 1948.

Physical exercises described and illustrated for women.

The Care of the Teeth. By G. H. Russell, M.B., Ch.B., L.D.S. (Pp. 48. 2s.) Altrincham: John Sheratt. 1948.

Instructions for the mother on the care of her own and her baby's teeth.

How to Become a Pharmacist. By W. A. Muteham, M.P.S. (Pp. 120. 5s.) London: The Actinic Press. 1948.

An outline for prospective entrants to pharmacy.

The Metabolic Brain Diseases and Their Treatment. By G. T. Stockings, M.B., B.S., D.P.M. (Pp. 262. 16s.) London: Baillière, Tindall and Cox. 1947.

The author discusses the physiology and chemistry of physical therapies and compares these with psychotherapeutic methods.

A Manual of Pharmacology. By T. Sollmann, M.D. 7th ed. (Pp. 1,132. 57s. 6d.) Philadelphia and London: W. B. Saunders. 1948.

Intended as a comprehensive outline of modern knowledge of pharmacology.

Sport und Kreislauf. Edited by Dr. A. Wander. (Pp. 154. 12.80 Swiss francs.) Bern: Medizinischer Verlag Hans Huber. 1947.

Papers on the circulatory system in relation to athletics.

La Streptomycine. By Prof. C. Levaditi. (Pp. 218. 350 francs.) Paris: Presses Documentaires. 1947.

A monograph on the preparation of streptomycin and its clinical and experimental applications.

Das Psychoanalytische Volksbuch. Edited by Federn and Meng. 4th ed. (Pp. 736. 24.50 Swiss francs.) Bern: Hans Huber. 1939.

An exposition of psycho-analysis for the layman.

Erkennung und Unterscheidung akuter innerer und ansteckender Krankheiten. By Prof. A. Sylla. (Pp. 456. R.M.18.) Berlin: Urban and Schwarzenberg. 1948.

A textbook of acute diseases and communicable diseases.

Melk in het bijzonder als Zuigelingenvoedsel. By Dr. J. H. de Haas and Ir. O. Meulemans. 2nd ed. (Pp. 112. No price.) Batavia, N.E.I.: Tweede Druk. 1940.

A monograph on the composition of milk.

Histopatologia d'una Nova Capa d'Epiteli Semiescamós pla que Cobreix les Mucoses Digestives. By F. D. i. Jorda. (Pp. 83. No price.) Barcelona: L'Institut d'Estudis Catalans. 1947.

An account of a "semi-squamous epithelial layer covering the gastric and intestinal mucosae" which the author claims he can demonstrate.

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THE PLEBISCITE RESULT

The present plebiscite, the results of which are analysed on another page, shows that the concessions made by Mr. Bevan have persuaded many medical men to change their attitude to the Act and their decision whether or not to enter the Service on July 5. In the plebiscite of February there was a 9 to 1 majority in an 84% poll against the Act. In this plebiscite approximately 2 out of every 3 doctors in a 77% poll disapprove of the Act, notwithstanding the concessions Mr. Bevan has made. The figures show that some of those who disapprove of the Act are nevertheless prepared to enter the Service on July 5. In answer to Question B—the most important question of the three—12,799 medical men in England and Wales and Scotland are in favour of accepting service, and 13,891 are not in favour. The group which answered this question contains those directly affected by the Act—consultants and specialists, general practitioners, and whole-time voluntary hospital workers. There is an almost even division of opinion—48% willing to enter the Service and 52% unwilling. The number of general practitioners (principals and assistants) against accepting service is 9,588. Although there is an overall majority against accepting service, the majority does not include approximately 13,000 general practitioners. The majority the B.M.A. required if it was to continue to advise the profession not to enter the Service has, therefore, not been obtained.

This *Journal* went to press while the Council met on Wednesday to receive the results of the plebiscite and to consider what action should be taken. While it may be agreed that the Council is faced with a difficult problem, Mr. Bevan is faced with one which is equally, if not more, difficult. Opinion as expressed in Parliament and in the Press welcomed his statement in the House of Commons on April 7 as being a real attempt to break the deadlock —an attempt, moreover, made in such a manner that showed Mr. Bevan was making a genuine attempt to conciliate those whom he had previously offended. His gesture, we suggested in a leading article in the *Journal* of April 17, warranted an equally generous response. The B.M.A. Council recognized the concessions made by Mr. Bevan, and in a temperately worded phrase stated that these concessions did not offer sufficient safeguards for the essential freedoms of professional life. The medical profession as a whole, in continuing to disapprove of the Act, supports the Council's view. In the last plebiscite each of the eighteen groups of medical men answering Question A disapproved of the Act in substantial proportions. In this plebiscite all except three of these groups still disapprove of the Act, though not so strongly as last time. Those approving include the salaried consultants or specialists, the whole-time teachers, and the whole-time research workers. But the majority of those employed whole-time in the Public Health Service still disapprove of the Act, and so by a very small majority do those working whole-time in Government service. A large majority of those holding permanent commissions in the Services are still in opposition. These facts cannot be ignored either by Mr. Bevan, or by the public, or by the medical profession.

In the last plebiscite 17,000 general practitioners were not prepared to enter the National Health Service. Those who still hold to this opinion now number 9,588. This figure falls far short of the 13,000 considered to be necessary in order to justify collective opposition to the Act, and the B.M.A. Council would therefore not appear to have a mandate to recommend such a course to the Representative Body. To organize collective opposition on such an insecure basis would be disastrous whatever the merits of the case. We are faced with the fact that over 7,000 general practitioners have changed their minds as a result of the concessions made by Mr. Bevan—and the fact that over 2,000 have not troubled to vote. It is possible that on further reflection more general practitioners will consider that while they have not gained all the points they sought the promised Amending Act and other concessions made by Mr. Bevan will provide them with an opportunity to practise their profession as independent men and women.

On the assumption that the Representative Body agrees that collective opposition is now out of the question it may decide that the best thing for the B.M.A. to do is to co-operate with the Minister of Health in trying to make the Service workable, to press for satisfactory terms and conditions of service for all sections of the profession, to be active in securing satisfactory Regulations, and to respond willingly to the Minister's invitation to assist him in framing the new Amending Act. If the B.M.A. pursues some such course in the interests of those who are prepared to serve under the new Act it will have no less an obligation to protect the interests of those of its members who decide to stay outside the Service. As there is a majority of Noes in answer to Questions A and B no one can pretend that the medical profession will enter this new Service in the enthusiastic manner which Mr. Bevan hoped would be the case. Apart from the deep antagonisms he stirred up in the medical profession by his treatment of the Negotiating Committee last December and his ill-advised utterances in the House of Commons in February, there is still a grave doubt in the minds of responsible doctors about the effect of a State medical service on the development of Medicine in this country. Whereas the voting in the plebiscite of February may have to some extent been influenced by a spirit of antagonism to the Minister of Health, we believe that this has had little influence in the results of the present plebiscite. Not only do medical men have serious doubts about the benefits to the public and to Medicine of a State medical service, but they have still graver misgivings about the possibility of starting such a Service in July in a way which is going to give the medical profession an opportunity to fulfil the promises made by the Government to the people of Britain Mr. Bevan has very

few bricks at his disposal to build his new house, and the foundations of it even are still in the main only architect's plans. We foresee endless confusion in the administration of this new Service, and foresee, too, that the public will express their disappointment in no uncertain manner. Much of this hostile criticism will fall unjustifiably on the heads of the doctors. The medical profession will be able to meet this, and compose differences of opinion within its own ranks, if it continues to preserve unity within diversity. Only by remaining united shall we be able to influence the development of the new Service and the framing of the new Amending Act promised by the Government.

THE CENTENARY OF PUBLIC HEALTH

On Thursday morning H.R.H. Princess Elizabeth opened the Health of the People Exhibition organized by the Central Office of Information, and sponsored by the Ministry of Health, which is designed to commemorate the centenary of the passing of the first great Public Health Act. On Friday evening the Corporation of London held a dinner to celebrate this same centenary and also that of the appointment of their first medical officer of health, Sir John Simon. On another page we publish an article which discusses the conditions which led to the passing of this Act, the accomplishments of the men who held the stage in these stirring times, and the course of sanitary reform in the years which immediately succeeded the new measures.

That the social conditions of the first half of the nineteenth century cried for redress is well known, but the significance of the increasing depths of degradation into which the poor of our cities were sinking is perhaps less appreciated. Although the cholera of 1832 disturbed the equanimity of the complacent it still needed the fulminations of Chadwick, combined with the inquiries of several official and unofficial committees, to bring home the simple fact that wretched social conditions mean disease and death, and that in the long run they do not pay. Thirteen years after the first outbreak of cholera the Health of Towns Commission gave illuminating figures for certain industrial towns. In Preston, for example, in the four-hundred-odd houses which were surveyed people were sleeping on an average three to a bed, and in 84 instances four persons shared the same bed. Three years later the Metropolitan Sanitary Commission presented a similar catalogue of vile conditions. Bermondsey was intersected by open ditches of the most disgraceful character, and in the streets of Whitechapel there was neither sewerage, drainage, cleansing, paving, nor a good supply of water. It was soon evident that the remedy for such conditions would conflict with vested interests. It was probably only a Chadwick—masterful, untiring, and self-sufficient—who could have brought these conditions home to the consciences of the legislators and owners. There was no house in the land which was not liable to suffer from the evils of sanitary defects. The Queen's apartments at Buckingham Palace were ventilated through the common sewer; and at Windsor Castle the footmen in the pantry suffered constantly from sore throats, till it was discovered in 1844 that there were more than fifty unemptied cesspools under the Castle.

From before 1832 reform had been in the air, but in the case of the health of the people it was an unconscionable time in coming. The Public Health Act of 1848 made up for the delay. This was a truly great and pioneer measure. It consists of 152 sections, and in its printed form takes up 67 pages. The preamble expressly indicates that the intention of the Act is to place under one and the same local management such functions as sewerage, drainage, cleansing, and paving. It constituted a General Board of Health and gave it power to appoint officers. The Act was permissive, but if any area had not adopted it, and a certain proportion of the inhabitants petitioned the Board regarding local conditions, the Board had power to order a local inquiry and, if the result was not satisfactory, to enforce the Act in that district by an Order in Council. A Local Board was given power to appoint officers, such as a Surveyor, an Inspector of Nuisances, a Clerk, and a Treasurer. The Local Board might also appoint a qualified medical practitioner as an "officer of health." There are important sections dealing with sewerage. The Local Board had power to purchase the rights vested in any person for the making of sewers, and were responsible for the repair of sewers vested in them. The Act also deals specifically with the drainage of houses, with water closets in factories, public conveniences, the keeping of swine, the keeping of slaughter-houses, the regulation of offensive trades, the registration of common lodging-houses, and the prohibition of the use of newly built cellars as dwelling rooms. There was a similar prohibition of the construction of any vault or grave within the walls of or under any church built after the passing of the Act. The nuisance clause—referring to drains, water closets, privies, cesspools, and ashpits—was advanced for its time, but the powers given for compulsory abatement were not adequate. From every point of view this Act, the centenary of which we celebrate this year, was an important and far-reaching measure.

We may refer briefly to the subsequent course of sanitary legislation in this country. There were of course many Acts of secondary importance, but these need not concern us. In 1866 the next principal Public Health Act was passed. This was not a permissive Act. As Simon expresses the matter, under it "the grammar of common sanitary legislation acquired the novel virtue of an imperative mood." By 1875 many Acts had been passed, and in that year all these were consolidated in the great Public Health Act, 1875. This was the long-abiding charter of health administration. It was not until 1936 that consolidation was again effected, and the Act of that year is still in force.

Turning to the other side of the picture, the translation of legislation into the day-to-day practice of the principles of sanitation, Dr. Underwood's article (p. 890) stresses the greatness of Simon in this field. Fortunate indeed was the City of London to acquire his services. At this time Duncan in Liverpool and Simon in London were the only two health officers in the country, and each in his own way was labouring, almost personally like a Hercules, to

cleanse the Augean stables of his area. It was eight years before medical officers of health were appointed for the vestries of the Metropolis, and later still for the country generally. The record of vital statistics shows what was achieved by these men in the succeeding years. At first the duties of these officers lay mainly in the field of sanitation, but from the days of Duncan and Simon, too, it had always been the function of the medical officer of health to deal in expert fashion with outbreaks of epidemic disease. This function could have been carried out only by a man qualified in medicine. As the years passed other clinical functions came within his field; to the supervision of tuberculosis was added the care of the mother, the school-child, and the infant, and in recent years cancer and rheumatism were tending to come under the jurisdiction of the health officer. Mr. Neville Chamberlain's Local Government Act, 1929—whose sole serious drawback was that it lacked the now by no means novel virtue of an imperative mood—enabled enlightened authorities to add to their responsibilities the maintenance and development of many large hospitals; and the medical officer of health had at last come into his own. His responsibilities now embraced the prevention and treatment of all diseases afflicting the seven ages of man.

The medical officers of health will regard these celebrations with pride—but pride mingled with regret and disappointment. Our legislators have seen fit to divorce hospitals from the health services, and once again the nation is faced with dual health administration. Yet the present generation of medical officers will look back with pride to the achievements of those men who in a true pioneering spirit shaped the public health service of this country to the great benefit of the health of the people of Britain.

HISTAMINE

It is becoming increasingly clear that drugs act by imitating or modifying the effect of substances which are ordinarily present in the body. The simplest illustration of this is the similarity between the drug ephedrine and the naturally occurring adrenaline. A large number of drugs imitate or modify the action of acetylcholine; they include muscarine, pilocarpine, arecoline, physostigmine, nicotine, and atropine. There is, in addition to adrenaline and acetylcholine, a third naturally occurring substance which like them is capable of producing dramatic effects in a moment—this is histamine. The function of this substance, unlike that of the first two, remains undiscovered, and we still think of it mainly as something toxic, which the body might well be without. In the lecture which is published in this issue of the *Journal* Prof. J. H. Gaddum has brought together all the clues which are available at the moment to those engaged in solving this riddle, and his analysis will be of the highest value to those working in this field.

It used to be thought that histamine was mainly produced in the lumen of the intestine, where bacteria made it from the amino-acid histidine by decarboxylation. It is true that some bacteria contain an enzyme which can carry out this change, but they do so only in an acid medium, about *p*H 5, and not in the alkaline intestine. Indeed, only when the bacteria have adapted themselves to an acid surrounding are they found to contain the enzyme. A further reason for regarding the intestine as an unimportant source of histamine is the fact that large doses of the substance have little pharmacological effect when taken by mouth; they are conjugated either in the lumen or in the wall of the intestine.

Gaddum discusses the formation of histamine and describes the important work carried out by Dekanski, who investigated the amount of histamine in mice. If a mouse is anaesthetized and then immersed in hot water the quantity of histamine in the animal is doubled in the following hour. The new formation appears to occur in the skin. Feldberg and Kellaway observed the discharge of histamine from perfused lungs produced by various agents and drew up a balance-sheet of the amount disappearing from the lungs and that appearing in the effluent; they obtained no evidence of new formation. According to an attractive theory put forward by Rocha e Silva, histamine is combined in the tissues in a peptide linkage between the -NH_2 group and the -COOH of lysine and arginine; the link is split by trypsin, with the setting free of histamine. The curious fact that the pain of a nettle-sting is caused by the simultaneous presence of histamine and acetylcholine has recently been demonstrated by Feldberg and Emmelin and is commented on in an annotation on another page. This action can be no coincidence, and must indicate a relation between the formation and function of the two substances.

If the body is flooded with histamine a large amount is excreted in the urine, but the enzyme histaminase is chiefly responsible for its removal. It has repeatedly been observed that there is a very great increase in the amount of this enzyme in the blood in pregnancy, which is believed to be due to production of histaminase in the placenta.

The best-known aspect of histamine at the present time is, however, the use of antihistamine drugs like "anthisan," "antistin," "benadryl," and others. One of the curious features of these substances is their apparent dissimilarity of chemical structure, which is so great as to suggest that their action cannot be related to their structure. Gaddum has made an interesting attempt to show how this difficulty may be overcome.

On other pages we publish articles on the clinical use of two of these compounds. Dr. J. Overton describes the use of antistin in skin conditions and Dr. N. Southwell the results of a trial of anthisan for asthma and hay-fever. Dr. Southwell's account is in some respects a model of how an investigation of this kind should be conducted. He furnished himself in the first place with dummy tablets as well as with tablets containing anthisan, and when he began to treat his patients he used the dummy tablets for the first two weeks in nearly all. He made the interesting observation that two patients with asthma of long standing found themselves notably benefited by these dummy tablets. The general method of the trial, which was carried on for eight weeks, was to grade each patient on his previous asthmatic history, and then to regrade him each week according to the severity of his attacks in the previous week. The grading consisted in allotting him a number from 1–6. At the end of the eight-week period the average weekly grading

number while taking the active preparation was available for comparison with the average weekly grading figure while taking the dummies. Needless to say the patients did not know whether they were receiving the real tablets or not.

The outcome of the trial was quite clear. Dr. Southwell found that anthisan—in a series of 27 patients—was of no benefit whatever in asthma, but that it was strikingly beneficial in hay-fever as shown in each of 15 patients. This investigation is an example of how a clinical trial can be made objective and quantitative, and it will well repay careful study by those faced with similar problems.

SURGEONS IN CAMERA

At a meeting of the Fellows of the Royal College of Surgeons held on April 28 three resolutions criticizing the National Health Service Act were passed. We observed in a recent leading article that it was desirable that the views of the Fellows of the Colleges on the National Health Service Act should be known. The Fellows of the Royal College of Physicians have already expressed their collective opinion in the two resolutions recently passed by the Comitia. Unfortunately the meeting at the College of Surgeons last week was held in secret and we were prevented from reporting it; a similar meeting a year and a half ago was open and was reported. The President of the College has, of course, the right to withhold an account of the meeting and to prevent publicity being given to the resolutions passed, which will presumably be considered at the next meeting of the Council of the College. But when between 200 and 300 Fellows meet at their own request to discuss such a serious matter as the National Health Service Act, and define their attitude to it in carefully considered resolutions, it would seem to be of the first importance that the medical profession at large should know the views of these distinguished men. The medical profession has urged upon the Minister of Health the need for free expression of opinion on all aspects of professional life and work in the new health service. It is regrettable that for the Fellows of the Royal College of Surgeons freedom of expression is to some extent curtailed by the withholding of their views from the rest of the medical profession. It is hoped that the Council of the College may remedy this by making public fairly soon the three resolutions passed on April 28. No good can come from concealing differences of opinion, and it is plain that consultants and specialists are sorely perplexed about their future under the National Health Service Act. This found expression in a resolution passed at a meeting of consultants in London two weeks ago. The Spens Committee's recommendations for consultants are not yet known, and Counsel's opinion (*Journal*, May 1, 1948) shows that many problems remain to be solved if consultants are to be able to work under the Act with anything like a contented mind.

THE ROYAL ACADEMY

In this age of statistics are there any to say how many doctors will be likely to visit the Royal Academy this year? It may be safe to say, quite unscientifically, that on the whole the medical profession is too busy for such pastimes as picture-gazing, although it is true that there are a number of reputable amateur artists among them. However, those who go to Burlington House this spring will have the pleasure of seeing Henry M. Carr's competent painting of the Council of the Royal College of Surgeons of England (279), which takes its place among the more formal exhibits. There is a portrait (467) of Miss Elizabeth Bolton, C.B.E., M.D., late Dean of the Royal Free Hospital School of Medicine, and here the artist, William Dring, has made bold use of the colours of the robe in a lively and penetrating study. E. Roland Bevan contributes a forceful bust of Sir Alexander Fleming, and Maurice Lambert an interesting and lifelike full-length portrait of Viscount Nuffield, the model of a statue to be executed in bronze for Guy's Hospital.

If doctors can put aside their Gray's *Anatomy* they may take some pleasure in André Dunoyer de Segonzac's masterly composition "Bathers" (663). In the same room Leslie Cole's "Seated Figure" (706) may tempt them to obstetric speculations. The psychologists among them, noticing the high incidence of vitamins in the subject matter of the smaller exhibits, may discover anew how emotion is deepened when the object becomes comparatively inaccessible, for among the most delicate colour harmonies and most painterly studies in the exhibition can be numbered Nancy Mellor's "The Midday Meal" (12), Alec Bailey's "The Flour Sack" (58), Robert Hurdle's "Round Table: Still Life" (268), and Margaret Noakes's "Still Life" (435).

In a more serious mood psychologists may also study the moving portrait of the late Mr. J. G. Winant (333), in which the artist, James Gunn, has caught behind the simple and rugged exterior a great depth of suffering.

"STROKE A NETTLE"

Anyone who is sufficiently provoked by the stinging nettle to wish to find out the cause of his discomfort will be able, thanks to N. Emmelin and W. Feldberg,[1] to obtain nearly a complete answer. The statement that the active principle of the nettle was formic acid has repeatedly appeared in print and become part of the lore belonging to the plant. It now appears that the juice of the nettle does not contain this substance in any measurable quantity. The facts are both more interesting than the fiction and more in keeping with contemporary biochemical research. It has been ascertained that the fluid in the hair of a nettle contains one part in a hundred of acetylcholine and between one part in five hundred and one part in a thousand of histamine. In the case of the former, the content of individual hairs could be pharmacologically estimated. Ten hairs from a stalk gave values ranging between 0.02 and 0.4 millionths of a gramme, with an average of 0.108. Hairs from the upper surface of leaves contained only about one-third as much. In so far as histamine is concerned it had been assumed in advance, not unreasonably, that the sting of a nettle hair would prove to be merely one more stimulus for the release of this substance from human tissues. Instead, the histamine came from the nettle, although it was necessary to pool the contents of some 15–30 hairs to obtain a measurable effect. Further, it was established by tests on human subjects that both the acetylcholine and the histamine are needed to provoke the typical reaction. Neither separately can produce the equivalent of a natural "sting." On the other hand indications were also obtained that nettle-hair juice produces a more marked effect than would be expected from its content of these two substances alone. It is suggested, therefore, that there is probably a third active principle, still unidentified but not formic acid.

[1] *J. Physiol.*, 1947, **106**, 440.

ISOLATION OF ANTI-PERNICIOUS-ANAEMIA FACTOR

Ever since the discovery by Minot and Murphy in 1926 that pernicious anaemia responds specifically to treatment with liver attempts have been made to isolate the responsible active principle. For many years it was believed that it was a member of the vitamin B complex, though Castle,[1] writing in 1945, could not identify it with any of the known members of the group. When Spies and his colleagues[2] found in 1945 that folic acid, which occurs in liver, restores the blood to normal in pernicious anaemia it was at first suggested that this might be the long-sought anti-pernicious-anaemia principle of liver. This view could no longer be held when it was shown that folic acid, unlike active liver extracts, failed to prevent the neurological complications of pernicious anaemia; indeed, some workers claimed that it appeared to precipitate them in certain patients. The anti-pernicious-anaemia factor of liver is also many thousands of times more potent than folic acid. Thus Clark[3] has calculated that, although 10 to 20 mg. of folic acid is the average daily dose needed for the initial treatment of pernicious anaemia, the maximum amount of it present in a curative dose of liver extract is of the order of 0.02 to 3.7 μg.—a 5,000- to 20,000-fold difference.

In 1942, three years before the isolation of folic acid, intensive research was begun by a group of workers in the Merck laboratories in America to isolate the anti-pernicious-anaemia factor from liver. After six years they now announce the preparation of small amounts of the factor in a pure crystalline form.[4] As the new factor is a member of the vitamin B complex, and as the last member to be named was B_{11} (later shown to be identical with folic acid), the American workers propose that the new factor be called vitamin B_{12}. The progress of the work was materially hastened by the discovery of Shorb[5] that a factor (LLD) required by the organism *Lactobacillus lactis* Dorner is present in refined liver extracts in concentrations bearing an almost linear relationship to the unit potency of the extracts used in the treatment of pernicious anaemia. It was suggested that the LLD factor might be the therapeutically active principle in these extracts. Intensive purification of clinically active liver fractions resulted in the isolation of a crystalline compound active for the growth of *L. lactis* and for the treatment of pernicious anaemia in relapse. This was vitamin B_{12}, which in doses of 3 to 6 μg. produced a prompt increase in the circulating reticulocytes, red cells, and haemoglobin in patients suffering from pernicious anaemia.[6] The haemopoietic activity of this preparation is thus 7,000 to 8,000 times that of folic acid. The discoverers believe that 1 μg. may be approximately equivalent to 1 U.S.P. injectable unit of liver. Clinical work with vitamin B_{12} has been hampered by the small amounts available.

During the last two years British workers have also been active in this field. As we reported in last week's issue of the *Journal*, Dr. E. Lester Smith,[7] of Glaxo Laboratories, describes in a recent issue of *Nature* the preparation by repeated chromatography of a gramme of two red pigments from four tons of proteolysed liver. The preparations are active in pernicious anaemia in doses of 20 μg., and, what is even more interesting, they are effective in the treatment of subacute combined degeneration of the spinal cord. Neither of Smith's pigments is identical with the vitamin B_{12} of the Merck group, since they are both amorphous and weight for weight are not quite so active clinically. Further developments are promised on both sides of the Atlantic, and they will be awaited with interest.

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[5] Shorb, M. S., Ibid., 1948, **107**, 397.
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[7] Smith, E. L., *Nature*, 1948, **161**, 638.

NEUROSIS AND RELIGIOUS DENOMINATION

Between thirteen and fourteen thousand Service men were admitted to the Sutton Emergency Hospital during the six years September, 1939–September, 1945; 9,354 men went into the neuropsychiatric wards and 4,202 into the general wards. Slater[1] has classified these patients by religious denominations. The classification was based solely on the men's statement given as a routine on admission to hospital. Over 70% belonged to the Church of England, and the ratio of admissions to the psychiatric wards to admissions to the general wards of men of this denomination was taken as a standard to compare with other religious groups. No denomination had a significantly lower ratio than that of the Church of England, all the significant differences being in those groups which had a greater tendency to neurosis. It might be mentioned, however, that in the case of the Church of Scotland the ratio was 0.775, but statistical analysis showed that this was not a significant result. The ratios of the groups having a significant difference were: Roman Catholics, 1.250; Methodists, 1.386; Salvationists, 2.843; Jews 5.338.

The interpretation of these figures can only be a matter of speculation, but Slater suggests that men of a neurotic disposition may find a particular denomination or religion attractive—for instance, the Salvation Army is not unwilling to gather in people with an irregular social record, among whom a high incidence of neurosis might be expected. The Jews are, however, in a different category, since nearly all the men were born into this faith and conversions to the creed are negligible. The Jews were unique among all the religious groups in showing a progressive rise in the incidence of neurosis during the course of the war. The number of admissions of Jews to the neurotic wards rose from 1.3% to 6.7% during the six years. This rise was not influenced by the recruitment of foreign refugees into the Army, all foreign nationals being excluded from the analysis. The author suggests that perhaps Jews possess a stronger than average attachment to their immediate domestic circle and the society of their fellows and that Army life causes a relatively greater strain.

[1] *J. ment. Sci.*, 1947, **93**, 392.

PROCEEDINGS OF THE ANNUAL MEETING

The Council of the B.M.A. has decided to publish in a separate volume the papers read before the Scientific Sections of the Annual Meeting to be held in Cambridge in June. Just before the war it was resolved that the Opening Papers read to the Sections should be published in the *Journal* at the discretion of the Editor. As the paper for the *Journal* is still strictly rationed, and as it is possible to find space for only a proportion of the original articles submitted in the ordinary way, it will be possible to print in the *Journal* only a few of the papers read at the Annual Meeting. But all contributions will be put on permanent record in the *Proceedings*. So that plans may be made for printing the *Proceedings* it is to be hoped that those who are reading papers at Cambridge in June will as soon as possible send them to the Editor of the *Journal*.

THE CENTENARY OF BRITISH PUBLIC HEALTH

RISE OF HEALTH LEGISLATION IN ENGLAND AND IN LONDON

BY

E. ASHWORTH UNDERWOOD, M.A., B.Sc. M.D., D.P.H., F.L.S.

Director of the Wellcome Historical Medical Museum

On May 7 the Corporation of London commemorated the centenary of the first Public Health Act and of the appointment of Sir John Simon as first Medical Officer of Health for the City. Although nowadays civic hospitality must be on a modest scale, the guests and the commemoration dinner were fully representative of the leaders in health legislation and administration and in the various departments of preventive medicine. The year 1848—the zero year of public medicine in this country—was marked by several events of the first importance, and this celebration, coinciding as it did with the opening of the Health of the People Exhibition, which has been arranged by the Central Office of Information and is sponsored by the Ministry of Health, was intended to commemorate all of them. This article is written as a reminder of these epoch-making events and as a tribute to the men, far-seeing beyond their time, who shaped their course.

The Prelude to Legislation

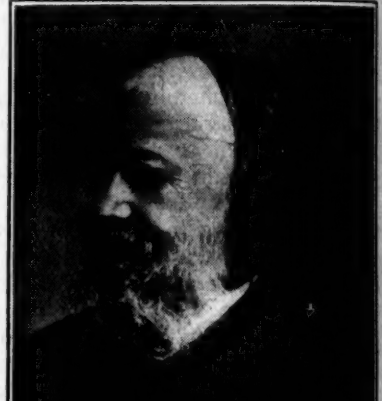
The cholera epidemic which ravaged this land in 1831–2 caused a profound but unfortunately temporary stirring of the social conscience of the people. The importance of this outbreak, and its effect on the minds of the men and women who feared its terrors, can hardly be overestimated. This disease of the Far East, which had hitherto been of interest only to those who had practised there, first reached this country in October, 1831, and from then until the end of 1832 it overran Great Britain and Ireland, causing the death of 31,400 persons in Great Britain alone. In a recent communication I gave a table showing the distribution of these cases in time (Underwood, 1948a), and it will be seen there that small towns appear in company with the great cities in this roll of dishonour. In 1833 there was a recrudescence of cholera in London, when the metropolis had 1,454 deaths, and there were also a few scattered minor outbreaks in other parts of the country. But for all practical purposes cholera had burnt itself out, and, although the fear of it continued to haunt the people, there was no further outbreak until the next great epidemic of 1848-9. The intervening period of sixteen years saw an armed truce between the forces of disease, filth, and squalor on the one hand and the powers which were being gradually assembled to combat them. No mean difficulty confronts anyone who sets out to give a few examples of the prevailing conditions. The reader may think that a finger of scorn is being pointed at a certain locality, whereas all the contemporary reports show that there was nothing to choose between any of them. With this proviso in mind a fairly typical example may be given here. Baker (1833) described some of the appalling sanitary conditions which were found in the township of Leeds. In three parallel streets, housing about 386 persons, the sanitary conveniences consisted of two small privies, which were in such a state as to be totally unusable. From the privies in one yard the accumulated filth of thirty years was removed by order of the Commissioners. Seven years after this cholera epidemic in Leeds the streets had again become so full of ashes, filth, and refuse of every description that their surfaces were far above their original level. It is small wonder that when official action was at last taken in this country generally it should have shown itself primarily in the abatement of sanitary nuisances. The broader conception of health measures began later, and evolved almost entirely in the mind of one man—Sir John Simon.

The cholera epidemic of 1831–2 had two results of the first importance. In the first place it showed the urgent need for a sweeping sanitary reform in town and country alike. In the second place it gave rise to an event which demonstrated that this reform, and the control of medical action against a grave epidemic disease, *could* be directed by a central government department. I refer to the Royal Proclamation of June 20, 1831, which announced the formation of a consultative Board of Health, of which Sir Henry Halford, the President of the Royal College of Physicians, was elected chairman (Simon, 1897). It was a matter for congratulation that this Board was appointed *before* cholera actually reached our shores. But it had no powers of compulsion, though the Government did subsequently issue certain Orders in Council implementing some of the Board's recommendations.

Though educated men and women felt the stigma of the conditions in which the population was dwelling, the stimulus to effect improvements was lacking, and the offensive weapons against the powers of darkness were not yet forged. The real awakening of the public conscience took place during the decade 1838–48. This was the era of Chadwick and Southwood Smith, of Neil Arnott and James Phillips Kay (Sir J. P. Kay-Shuttleworth). The necessary action came through a demand for the reform of the Poor Law, and it is worth while noting that ten years were to elapse between the recommendation for the introduction of the necessary legislation and the actual passing of the Act.

Sir Edwin Chadwick

Edwin Chadwick (1800–90) was one of those men who stumbled almost by accident into their life's work. As a young man he studied for the Bar, but when he was 29 years old he wrote an essay on *Preventive Police* which was seen by Jeremy Bentham. The two men met and appear to have got on very well together, since Chadwick went to stay with Bentham at the latter's house in Queen's Gate. The association continued until Bentham's death in 1832, and during the intervening period Chadwick was called to the Bar, carried out many first-hand investigations into the social conditions of the poor in London, and finally renounced the Bar as a profession. The reason was his appointment in 1832 as an Assistant Commissioner to the Commission which had been set up to inquire into the Poor Law system. In the following year he was promoted to be a Commissioner, and in the same year he was also appointed as one of the three Commissioners on a Royal Commission to examine the treatment of children in factories. In 1834 the Poor Law Commission issued its Report, and this led to the Poor Law Amendment Act and the formation of the Poor Law Board with Chadwick as secretary.



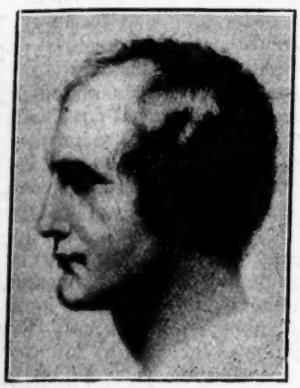
Sir Edwin Chadwick, 1800–90

Chadwick really opened his campaign against the evils of defective sanitation four years later, when the Poor Law Board sent a famous letter to Lord John Russell, the Home Secretary, in which they pointed out that some of the most important charges on the poor rates are those "which are caused by nuisances by which contagion is generated and persons are reduced to destitution." Later on the Commissioners said: "We have eagerly availed ourselves of the opportunity of making the present Report, to submit to your Lordship the urgent necessity of applying to the Legislature for immediate measures for the removal of these constantly acting causes of destitution and death. All delay must be attended with extensive misery, and we would urge the consideration of the fact that in a large proportion of cases the labouring classes, though aware of the surrounding causes of evil, have few or no means of avoiding them, and little or no choice of their dwellings."

Southwood Smith

The Commissioners attached to their letter two reports which had been specially drawn up by their medical inspectors. The first was a joint report by Dr. Neil Arnott and Dr. James Phillips Kay, *On the Prevalence of Certain Physical Causes of Fever in the Metropolis.* Neil Arnott (1788–1874) was at that time a well-known London physician and was a physician-extraordinary to the Queen. In 1827 he wrote a popular textbook on physics, and his practical inventive capacity found expression in such well-known devices as Arnott's ventilating valve, his smokeless fireplace, and his water-bed. Arnott was a founder and an original member of the Senate of the University of London (1836). Sir J. P. Kay-Shuttleworth (1804–77) became secretary to the Manchester Board of Health, and was the author of a technical work on asphyxia. He may be regarded as the founder of English popular education, and he was a joint founder of Battersea Training College.

More intimately connected than either of these men with the succeeding progress of legislative public health was the author of the second report attached to the Board's letter—Thomas Southwood Smith (1788–1861). Munk gives a sympathetic summary of his life and work (Munk, 1878). Smith was at first a dissenting minister in his native Somersetshire, and he then studied medicine at Edinburgh. During this period he wrote his *Divine Government,* which was praised among others by Byron, Moore, and Wordsworth. Southwood Smith was for twenty-four years physician to the London Fever Hospital, and he was therefore well qualified to carry out medical work for the Poor Law Board. This second report to which I have referred was entitled *On Some of the Physical Causes of Sickness and Mortality to which the Poor are Particularly Exposed.* It emphasized the fact that, while in the districts of London occupied by the wealthier classes streets had been widened, drainage improved, and nuisances removed, nothing whatever had been done to effect similar remedies in the poorer districts. He gave telling figures to emphasize the results. Southwood Smith was later prominent in the formation of the Health of Towns Association (1839) and of the Metropolitan Association for Improving the Dwellings of the Industrial Classes (1842). His essay (1832) in the *Westminster Review,* which was later reprinted as a pamphlet entitled *The Use of the Dead to the Living,* led to the passing of the Anatomy Act. He wrote also on fevers and a popular work entitled *The Philosophy of Health* (1835–7). To anticipate, Southwood Smith became the medical left hand to Chadwick's right. When the General Board of Health was constituted in 1848 Southwood Smith became its medical member, and he remained in this office until the Board was dissolved in 1854. It is well known that he was Jeremy Bentham's private medical attendant; that Bentham left his body to Smith for dissection; and that Smith delivered an oration over the body on June 9, 1832, before starting the dissection.



Thomas Southwood Smith, 1788–1861

Chadwick's Harvest Years

The letter from the Poor Law Board to the Home Secretary led to many debates in Parliament, especially in the House of Lords, and in 1842 the Government published three volumes of reports. The third volume was entitled a *General Report on the Sanitary Condition of the Labouring Population of Great Britain.* It was written by Chadwick, and was published (1842) in his name. He recommended, *inter alia,* efficient drainage, the removal of refuse, and the improvement of water supplies. He also made the prophetic statement that "it would be good economy to appoint a district medical officer independent of private practice, and with the securities of special qualifications and responsibilities to initiate sanitary measures and reclaim the execution of the law." Chadwick's recommendations were substantially confirmed by a Royal Commission which reported in 1844 and 1845 and gave thirty detailed recommendations proposed for the local authorities. The chief momentum for all subsequent action came from this report of Chadwick's and from the Report of the Health of Towns Commission which soon followed.

The years 1845-7 saw the placing on the Statute Book of a number of minor measures—dealing with markets and fairs, gas-works, waterworks, and cemeteries—which formed the background to the Act of 1848. This was the Public Health Act, which received the Royal Assent on August 31. This is the charter which is being celebrated this year. Another important measure was the Nuisances Removal and Disease Prevention Act of 1848. A metropolitan Act of 1848 made similar provisions for London as did the Public Health Act for the rest of the country. (This London Act did not apply to the City, which was dealt with by the City Sewers Act.) The new legislation established a system of summary jurisdiction against the chief health nuisances. It further created a General Board of Health, which was to continue for five years. Chadwick was appointed one of the three Commissioners, along with Lord Carlisle and Lord Shaftesbury. A little later Southwood Smith also became a member of the Board. The addition of Smith did not occur until 1850, and on the authority not of a Public Health Act but of the Metropolitan Interments Act. This led Henry Wyldbore Rumsey (1856) to write of the whimsical experiment which had been tried of appointing three non-medical authorities—two lords and a barrister—to preserve the health of the living, and then, after a year or so of doubtful success, of calling in a physician to bury the dead.

Under the driving force of Chadwick the new Board got rapidly to work. By 1853 the Board had been memorialized from 284 places for application of the Act, and had applied the Act in 182 places having in all more than two million inhabitants. The Board introduced measures regarding common lodging-houses, and made recommendations regarding burials in towns. In the field of water supply it straightway developed grandiose ideas. It proposed to centralize all the water undertakings of London, and there is evidence that it intended to be itself the owner and director of this organization. There is no doubt that this first General Board of Health laboured from the start under three drawbacks. In the first place, it was not represented in Parliament by a Minister of the Crown, so that criticism of its activities could not be dealt with effectively as soon as it was uttered. Secondly, it had no whole-time engineering inspectors. Its technical experts were engaged in the locality where they were to be temporarily employed, and in this way abuses were apt to be met with. The third drawback was—Mr. Chadwick. As a pioneer he had been admirable, but the very qualities which made him a great pioneer rendered him rather intolerant as an administrator. If there were vested interests which *might* be trod on Chadwick trod on them with all his weight. The result could not have been long in doubt. In 1854 the General Board of Health was terminated and a new Board was constituted in its place. Chadwick retired on a pension of £1,000 a year. His "official" life was ended, but during the next thirty-five years he continued to wage an unofficial war on dirt and disease. As an administrator Chadwick was impatient of results. In Sir John Simon's words, "he probably hoped to achieve in a few years the results which not ten times his few years could see achieved; and where others on all sides were hanging back, his ardour seemed ready to undertake the work of all."

In passing, it should be said that the General Register Office had been established in 1836, and that William Farr had been appointed as Compiler of Statistics in 1839. Farr founded a new science. In the telling phrase of Simon, he was "a master of the methods by which arithmetic is made argumentative." One has either to write much about him, or exclude him of design, and honourably. In this short note I have no choice. His work was an essential weapon for his contemporaries and many who followed later. To those who are interested I would recommend the sympathetic account of his mind and work which Prof. Greenwood (1948) recently published.

The Rise of the Medical Officer of Health

I have already quoted Chadwick's words recommending that it might be worth while to appoint whole-time medical officers

independent of private practice. An Act of 1847—the Towns Improvement Clauses Act—not only dealt with improvements in paving, draining, cleansing, and lighting, but gave power to large towns to appoint such medical officers. Liverpool had already anticipated this authority, since it had by a local act of 1846 sought and obtained power to appoint a medical officer of health. Dr. William Henry Duncan—the first medical officer to be appointed in Great Britain—had taken up office on Jan. 1, 1847. Duncan was a most conscientious and capable officer, and in Liverpool he had to deal with incredible problems of overcrowding, bad sanitation, gross immigration, and constant outbreaks of disease. If his reports did not have the classic ring of those of Simon, he was nevertheless a great medical officer who demands our respect. In another communication I deal more fully with his work (Underwood, 1948b), and Prof. Frazer, of Liverpool, recently published a biography of Duncan which was long overdue.

The City of London followed swiftly the example set up by Liverpool. The City Sewers Act of 1848 was to become operative from Jan. 1 of that year. It contained important provisions relative to the sanitation of the City, and gave power for the appointment of a medical officer of health. In October, 1848, Simon took up this office.

Sir John Simon (1816–1904)

The holder of this important post was a young man who was well fitted by his training and general intellectual ability to fill it with dignity. John Simon, born in 1816, was the sixth of fourteen children, and was more than half French. At 16 years he studied in Germany for a year, and in 1833 he was apprenticed to the surgeon Joseph Henry Green. Qualifying in 1838, Simon decided on a surgical career, and during the next ten years he held posts of some importance as a surgeon and as a pathologist. For his pathological work he was elected to the Royal Society at the age of 29, though the mesh was much wider then than it is now. In his spare time he studied metaphysics, Oriental languages, and art.

Sir John Simon when Medical Officer of Health, City of London, 1848–55

Simon held the post of medical officer of health to the City for seven years. When the new General Board of Health was formed Simon became its first medical officer in 1855. Shortly afterwards the Board's duties were taken over by the Privy Council, and Simon served this body well for thirteen years. Supported by a brilliant team of colleagues, he built up a system of public health which was the envy of the world. He was in effect preaching the importance of public health as an administrative entity, and the creation of a Ministry of Health. In 1871 his hopes were dashed when various heterogeneous departments were amalgamated to form the Local Government Board. Public health interests were now constantly subordinated to the demands of the Poor Law, and the advice of medical officers to that of lay administrators. In 1876 he asked leave to retire, and the country thus lost one of its ablest administrators while he was still an active force. After his retirement Simon lived for 28 years—the recipient of many honours and the friend of many celebrities, including Ruskin and George Henry Lewes.

Simon at the City

The office of medical officer of health to the City of London was of great importance in 1848, as Simon very soon found. He came to be regarded at Whitehall as an officer available for the general public service, and he served on several important Government bodies. On his appointment Simon at once came to an arrangement with the Registrar-General whereby he was provided each Monday with the death returns for the City for the previous week. He instituted a system of weekly inspections, with a follow-up of all nuisances. In the few years of his tenure of the office enormous improvements were effected in drainage, water supply, the abatement of nuisances, in scavenging, and in general cleanliness. He says himself that "at a time when cesspools were still almost universal in the Metropolis, and while, in the mansions of the west-end, they were regarded as equally sacred with the wine-cellars, they had been abolished, for rich and poor, throughout all the square mile of the City."

The five annual reports which Simon wrote while he was at the City are classics of public health administration. In his first report he pointed out that the mortality was about twice the mean mortality of surrounding districts. He stated that some thousands of houses in the City still had cesspools, and he described their evils in eloquent language. In dealing with water supply he laid down the postulates that every house, and every floor of a tenement, should be separately supplied; that every privy should have a sufficient supply; that every court should have a standcock; and that the supply should always be uninterrupted. He stated that there were 138 slaughter-houses in the City, and in 58 of these slaughtering occurred in vaults and cellars. He was convinced that both slaughter-houses and other offensive trades should be excluded from the Metropolis. He not only condemned further burial in vaults but recommended the burial outside the City of coffins already deposited in vaults. In connexion with unfit and unsanitary houses he struck a modern note immediately: the removal of walls is, he says, only a palliative, and the best measure is the wholesale purchase of series of courts and the demolition of all the houses in them. In dealing with the social conditions of the poor he expresses his belief in the powers of education. Simon emphasized that the most important task which lay ahead was inspection, and he recommended the establishment of a whole-time staff of inspectors. Finally he said that he considered it indispensable that the authority should receive the largest and most accurate returns which could be procured of *all sickness* occurring among the poorer classes. A hundred years after he wrote these words these returns are still indispensable for both the statistician and the administrator—but they have not yet materialized. Simon's other reports followed closely on the lines of his first—emphasizing water supply in one year, cholera in another, as the occasion demanded. As examples of vigorous, fearless prose in official reports they can seldom have been equalled.

Epilogue

The events which I have inadequately described had a far-reaching influence in this country and abroad. The two men who were principally concerned were both young men when they entered the field, and both were pushed out of office while still in mature manhood. Simon qualified in 1838, and during the decade when Chadwick was at his prime Simon apparently showed not the slightest interest in what was going on in the field of sanitation and public health. Yet in 1848 he took over the most important area in the country, wrote a classic report, and immediately laid down plans of action and procedure which were to be followed by other health administrators for many years to come. While during these centenary celebrations we will honour them and their only slightly less gifted colleagues, our thanks are also due to the enlightened members of the City Corporation in 1848–54—for these were the men who first really accepted Chadwick's principles and who gave Simon the opportunities which he so quickly grasped.

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PLEBISCITE ON THE NATIONAL HEALTH SERVICE ACTS

Summary and analysis of replies received up to and including 3, May, 1948

TABLE I

(1) Reference to Plebiscite Form	(2) Classification of professional work	(3) Registered medical practitioners either resident in Great Britain or serving in H.M. Forces at home (54,667 plebiscite forms issued)						Classification No.
		England and Wales		Scotland		Total Great Britain		
		Approve	Disapprove	Approve	Disapprove	Approve	Disapprove	
A	1a. Consultant or specialist, not holding whole-time salaried post	1,068	2,526	168	274	1,236	2,800	1a
I APPROVE of the National Health Service Act, 1946, in view of the modifications now proposed by the Government.	1b. Consultant or specialist, holding whole-time salaried post	787	530	132	74	919	604	1b
	2. General practitioner, principal ..	4,679	9,802	765	1,040	5,444	10,842	2
	3. General practitioner, assistant ..	629	1,144	158	173	787	1,317	3
	4. Whole-time voluntary hospital ..	1,010	1,593	208	278	1,218	1,871	4
I DISAPPROVE of the National Health Service Act, 1946, notwithstanding the modifications now proposed by the Government.	5. Whole-time local authority general hospital	474	517	62	55	536	572	5
	6. Whole-time local authority special hospital	361	341	60	88	421	429	6
	7. Whole-time public health service ..	784	883	102	120	886	1,003	7
	8. Whole-time Government service ..	255	290	68	52	323	342	8
	9. Whole-time teacher	219	151	50	65	269	216	9
	10. Whole-time research	149	103	24	20	173	123	10
	11. Other whole-time non-Government post	151	207	21	34	172	241	11
	12. Medically qualified dental surgeon	19	199	15	45	34	244	12
	13. Retired	638	2,321	127	295	765	2,616	13
	14. Unclassified	695	1,297	135	227	830	1,524	14
	Totals	11,918	21,904	2,095	2,840	14,013	24,744	
	15. Services, permanent commission					179	410	15
	16. Services, temporary commission, specialist					53	69	16
	17. Services, temporary commission, graded specialist					88	106	17
	18. Services, temporary commission, general duty officer					287	513	18
	Totals ..					14,620	25,842	

TABLE II

B		In Favour	Not in Favour	In Favour	Not in Favour	In Favour	Not in Favour	
I AM in favour of accepting service under the National Health Service Act, 1946, in view of the modifications now proposed by the Government.	1a. Consultant or specialist, not holding whole-time salaried post	1,347	2,148	234	197	1,581	2,345	1a
	1b. Consultant or specialist, holding whole-time salaried post	916	360	161	42	1,077	402	1b
I AM NOT in favour of accepting service under the National Health Service Act, 1946, notwithstanding the modifications now proposed by the Government	2. General practitioner, principal ..	6,586	7,757	1,050	736	7,636	8,493	2
	3. General practitioner, assistant ..	808	957	195	138	1,003	1,095	3
	4. Whole-time voluntary hospital ..	1,249	1,328	253	228	1,502	1,556	4
	Totals	10,906	12,550	1,893	1,341	12,799	13,891	

TABLE III

C		Agree	Do Not Agree	Agree	Do Not Agree	Agree	Do Not Agree	
I AGREE to abide by the decision of the majority and undertake not to enter the Service if the answers to Section B reveal a majority against undertaking service as defined in paragraph 4 above and if so advised by the British Medical Association.	1a. Consultant or specialist, not holding whole-time salaried post	2,589	850	257	154	2,846	1,004	1a
	1b. Consultant or specialist, holding whole-time salaried post	487	717	73	121	560	838	1b
	2. General practitioner, principal ..	9,506	4,413	979	748	10,485	5,161	2
	3. General practitioner, assistant ..	1,202	516	189	122	1,400	638	3
I DO NOT AGREE to abide by the decision of the majority if it is against accepting service as defined above in paragraph 4.	4. Whole-time voluntary hospital ..	1,590	928	307	167	1,897	1,095	4
	Totals	15,374	7,424	1,814	1,312	17,188	8,736	

The work carried out by staff of the British Medical Association for the purpose of obtaining a plebiscite of the medical profession on the matters set out in column (1) of the above Tables was directed and supervised by our representatives continuously from its start on 16, April until 4, May, 1948. The completed plebiscite forms received during that period were examined only by our representatives and by staff of the Association working under our supervision and under pledge of secrecy and were retained under our control from the time of their receipt at B.M.A. House until their destruction in the presence of our representative on 4, May, 1948.

We satisfied ourselves by appropriate tests

(1) that all reasonable steps were taken to furnish a plebiscite form to every registered medical practitioner either resident in Great Britain (but not Northern Ireland) or serving in H.M. Forces at home ;

(2) that the figures set out in the foregoing Tables I, II, and III are a correct summary and analysis of the replies received at B.M.A. House up to and including the second post on Monday, 3, May, 1948.

3, Frederick's Place,
Old Jewry, London, E.C.2.

PRICE, WATERHOUSE & Co.
Chartered Accountants.

4, *May*, 1948.

PLEBISCITE RESULTS, MAY, 1948

SOME IMPORTANT PERCENTAGES

All percentages are calculated to the nearest whole number. 50,514 Plebiscite Forms were sent to practitioners other than those serving in H.M. Forces. The distribution of practitioners as between England and Wales and Scotland* is based on figures obtained from B.M.A. records.*

		Question	Total Voting	Percentage Approving the Act	Percentage Disapproving	Not Voting	Of those who Voted	
							Approving	Disapproving
All civilian categories	Great Britain	A	77%	28%	49%	23%	36%	64%
	England and Wales* ..	A	78%	28%	50%	22%	35%	65%
	Scotland*	A	70%	30%	40%	30%	42%	58%

	Question	Of those who Voted	
		(A) Approving (B) In Favour (C) Agreeing	(A) Disapproving (B) Not in Favour (C) Not Agreeing
Group 1 A. Consultant or specialist not holding whole-time salaried post	A	31%	69%
	B	40%	60%
	C	74%	26%
Group 1 B. Consultant or specialist holding whole-time salaried post	A	60%	40%
	B	73%	27%
	C	40%	60%
Group 2. General practitioner principal	A	33%	67%
	B	47%	53%
	C	67%	33%
Group 3. General practitioner assistant	A	37%	63%
	B	48%	52%
	C	69%	31%
Group 4. Whole-time voluntary hospital†	A	39%	61%
	B	49%	51%
	C	63%	37%

† Excluding those of specialist status (covered by Group 1 B) but including practitioners holding B1, B2, and A appointments and Class I and Class III appointments under the Government's postgraduate scheme for ex-Service practitioners.

Reports of Societies

ENDOCRINOLOGY OF SCHIZOPHRENIA

In the Section of Psychiatry of the Royal Society of Medicine on April 13, with Sir DAVID HENDERSON presiding, certain experimental investigations of the endocrinology of schizophrenia were presented.

Dr. R. E. HEMPHILL said that the theories he put forward were advanced with the greatest diffidence. It was not his intention nor that of Dr. Reiss, who was associated with him in a research programme, to suggest that schizophrenia was an endocrine disorder, but from their work and that of others there was sufficient evidence to encourage research into endocrine relationships. The greatest single difficulty in research of this character was to find case material which was clinically homogeneous. An endeavour had been made to collect cases on account of their psychiatric similarity, but it was found that cases which had an apparently identical picture clinically might have dissimilar physiological patterns. The majority of the papers on the subject had dealt with the investigation of phenomena in isolation, such as oxygen consumption, liver function, and so on, and to add to the multitude of such investigations could contribute little to the problem. Therefore the present research had been directed to biological or endocrine indications.

In recent years pathological changes in the testes in schizophrenia had been studied. Biopsy specimens consistently showed an abnormal picture in schizophrenia. The speaker proceeded to describe a series of tests, but remarked how strongly the picture of inconstancy operated against biochemical research. It had been thought that schizophrenic patients could be grouped into those of constant and those of inconstant physiological or biochemical patterns, but unless the patients were in the same stage of the disease or were suffering from the same conditions clinically much variation in the results was to be expected. If tests could be devised which would reveal constancy or inconstancy it should be possible to detect patients with similar patterns and subject them to extensive and detailed investigations.

Study of Ketosteroids

A special study was made of the ketosteroids for constancy and inconstancy as well as for information about endocrine activity. It was observed that their output increased after electrical shock treatment and leucotomy. After E.C.T. a sudden increase up to three times the upper level of normal had been seen; but it was still impossible to isolate from these results any particular pattern of variation, and it could not be said that the patients could be grouped according to constancy and inconstancy patterns. After further study a group of six chronic patients who had failed to respond to recognized treatments were chosen, first because they were regarded as incurable, secondly because it was possible to assess their clinical state by a mere inspection, and thirdly because the onset of their illness occurred in each case rather late in life, and thus it was hoped to avoid the variation of the endocrine changes in early adolescence. They were as nearly similar in health, nutrition, and clinical picture as possible, and were investigated under standard conditions. But although these patients were identical clinically the fractionated ketosteroids were not. Dr. Hemphill described one case in which treatment daily with testosterone brought about a remarkable clinical improvement. The patient, aged 33, who had scarcely spoken for eight

years, and had been immobile, became active, talking and walking, and showed an increase in weight and growth of beard. Although this patient did not recover, he remained for a year in a state of partial remission, only relapsing if not treated with testosterone. The patient's state was not corrected, but it was influenced, and it was reasonable to suppose that in this single case there was a close relationship between the abnormal endocrine state and the clinical condition. Without biochemical control the empirical treatment of these patients would have produced the same result, but it would not have been possible to say why treatment succeeded in the one case and not in the others. One could not optimistically speculate that if the methods of analysis were sufficiently correct definite indications for treatment in many cases could be found; endocrine diseases were not simple, and might have to be corrected by the administration of more than one hormone. Nor was it known whether the successful result was due to the direct action of the hormone or to its effect on the hormone balance. The necessity of prolonged treatment had been stressed by other workers.

Another investigation related to thyroid function. A proportion of schizophrenic patients responded to thyroid treatment for a time, and many showed a tolerance of thyroid for a few weeks, but it was not clear whether these results were due to failure of reactivity or to some special property of the thyroid itself. Investigations had also been made concerning the physical development of schizophrenic patients, and these would be continued for five years and records of the measurements kept.

The speaker touched finally on puerperal schizophrenia. In such cases the pre-psychotic mental constitution was usually good and the physique normal, and this was the one form of schizophrenia which came under treatment within a few days or weeks of the onset of psychotic symptoms. The prognosis on that basis seemed likely to be favourable, but in point of fact the prognosis was probably the worst of all, and in his service there appeared to have been not more than two or three cases of puerperal schizophrenia which had made full remission. Puerperal schizophrenia should be an entity in the disease group and most acceptable to hormone investigation.

Other Investigations

Dr. M. REISS added a number of further points on investigation and described in more detail the experiments outlined by Dr. Hemphill. He said that it seemed clear that there was something decidedly wrong with the adrenal mechanism in these patients, sometimes a lowered, sometimes a heightened function. He described the difficulties of estimation of thyroid function in schizophrenia until there was worked out a modification of the method recommended by Dr. Russell Fraser and it was possible to determine in certain cases the protein-bound iodine. There were very few results to date, but, such as there were, they were in the same direction as the results with the ketosteroids. Very often there was a decrease of the protein-bound iodine, but sometimes a very considerable increase. Concerning the pituitary hormones, the problems were mainly those of method. It might be asked how a disturbed state of the anterior lobe function could have an effect on the brain. From one-third to one-fourth of the total metabolism in the body took place in the brain, whose sugar reserves were quickly exhausted. Dr. Reiss added that nothing was more easy or tempting than to form hypotheses, particularly if facts were few and not contradicted, but it was much more profitable to leave any hypotheses and just to see what future developments would bring.

EPIDEMIOLOGY OF TRYPANOSOMIASIS

At a joint meeting of the Section of Comparative Medicine of the Royal Society of Medicine and the Royal Society of Tropical Medicine and Hygiene, held on April 21 under the chairmanship of Mr. R. E. GLOVER, a discussion took place on the epidemiology of trypanosomiasis in animals and man.

Mr. J. CARMICHAEL said that tsetse flies were confined almost entirely to the continent of Africa. Generally speaking, the existence of domestic animals was incompatible with contact with the fly. The dwarf cattle of West Africa were apparently able to survive, and it had been claimed that this particular breed was immune, but absolute proof of immunity had not been obtained even after ten years' work on the problem by the Agricultural Department in Nigeria. Large numbers of human beings in Africa were living in contact with the tsetse fly, and the question was whether the fly was infected with the human parasite and, if it was, why the disease did not occur. Even under epidemic conditions the percentage of infection was never very high. Why was it that over large parts of the area domestic animals were infected but not man? He could not help thinking that throughout Africa there must be a balance between trypanosomes and man, and that this balance was upset and an epidemic started as a result of some outside factor, environmental or nutritional. A great deal of fundamental knowledge was still lacking. During a sojourn in the West Nile many years ago he had noticed the occurrence of epidemics following periodical famines. Treatment of cattle by means of drugs in the tsetse fly areas was a waste of time because the cattle were quickly reinfected. One of the most important factors in the epidemiology of trypanosomiasis, whether in man or animals, was the shifting character of the fly population. In Uganda, where he had first-hand experience for many years, the extension of the fly area recently had been most serious.

Dr. C. A. HOARE said that trypanosomiasis as affecting both man and domestic animals afforded one of the best examples of common ground between medical and veterinary science. Both the epidemiologist and the protozoologist were faced with the same problem—detection of the source of infection and its control. The parasites supposed to be responsible for the chronic and acute forms of sleeping sickness were *T. gambiensis* and *T. rhodesiensis* respectively, but these two parasites were closely related and sometimes apparently identical. The question of reservoir hosts was highly controversial. From the epidemiological point of view trypanosomes found in animals in localities where the human disease was unknown were probably *T. bruceii*.

In addition to epidemiological data, significant results throwing light on the problem had been obtained from observations on experimental infections in various animals. It had been demonstrated that *T. rhodesiensis* could be maintained by cyclical transmission to antelopes and to sheep for about ten years, in the course of which it remained infective for man. Similar observations on *T. gambiensis* showed that it could be transmitted cyclically to goats and pigs for four years without losing its transmissibility to man. It was concluded that in sleeping sickness various other mammals in addition to man constituted a source of infection, and that the relative importance of the human and animal reservoirs differed according to the type of distribution of the disease.

If it were proved that *T. bruceii* were capable of establishing itself in man, both wild animals harbouring this trypanosome and domestic animals would have to be reckoned as dangerous sources of human infection. Apparently the chief factor which prevented *T. bruceii*—from which there was reason to believe human trypanosomiasis had originated—from establishing itself in man was the trypanocidal action of normal human serum; but as human serum might occasionally lose its trypanocidal properties, as, for example, in some diseases of the liver and in certain types of avitaminosis, some workers maintained that human beings with such conditions might become susceptible to *T. bruceii*. Further, exceptionally virulent strains of *T. bruceii* might be capable of overcoming the trypanocidal action of normal human serum. According to this hypothesis, having thus established itself in man, *T. bruceii* would gradually adapt itself to its new host, at first behaving like *T. rhodesiensis*, with which it had so many features in common, and would give rise to acute disease, and subsequently adaptation would continue to improve and the trypanosome would acquire the characteristics of *T. gambiensis*, giving rise to a mild or chronic disease. Although on theoretical grounds this appeared to be a plausible hypothesis, it could not be accepted unreservedly, for several reasons. All attempts to infect human volunteers with *T. bruceii* had so far failed, though in a case recently reported from the Belgian Congo a transitory infection had been produced. It had also been demonstrated that *T. rhodesiensis* could be transmitted cyclically to ruminants for many years without losing its power to infect man—in other words, without reverting to a form indistinguishable from *T. bruceii*. It

might be concluded that *T. bruceii* could not readily adapt itself to man unless it was transformed into *T. rhodesiensis*. It was reasonable to assume that this evolution had actually occurred in the remote past and might operate at present under exceptionally favourable conditions, the nature of which was not yet known.

In conclusion it might be noted that in addition to trypanosomes which were common to man and the lower animals, like the African and South American trypanosomes, there were a large number of cases on record showing that purely animal parasites could occasionally break the barrier of host restriction and establish themselves primarily in man. On one or two occasions human infection with the trypanosome of ungulates had been reported from Africa.

In the course of a short discussion Dr. J. T. EDWARDS mentioned with regard to non-tsetse trypanosomes the difference in susceptibility to infection of different species of animals. In India horses which became infected with a particular trypanosome almost invariably died, whereas cattle were highly resistant, though probably carriers. In the chemotherapy of trypanosomiasis in horses treatment had to be drastic, for if one surviving trypanosome were left in the animal there would be a relapse.

BACKACHE–SCIATICA SYNDROME

A joint meeting of the Liverpool Medical Institution and the Manchester Medical Society, held at Liverpool on March 4, discussed "The Backache–Sciatica Syndrome and the Intervertebral Disk."

Sir HARRY PLATT reviewed the stages by which our present knowledge of the pathogenesis of the backache–sciatica problem had been reached. During the past forty years the concepts of sacro-iliac and lumbo-sacral strain, the part played by lumbo-sacral skeletal anomalies, the intervertebral arthritis theory, and the contracted ilio-tibial band represented a sequence of clinical entities which had in turn been rejected in favour of the present-day view that the prolapsed intervertebral disk was a dominant lesion in sciatica. He referred to the many thousands of successful operations for the relief of backache–sciatica which had been carried out by neurological surgeons and orthopaedic surgeons both in Great Britain and the U.S.A. On the other side of the picture, however, was the experience of a not inconsiderable number of failures to demonstrate a disk lesion at operation. Moreover, extravagant claims had been made for the intervertebral disk as the only "reputable" cause of sciatica. Many now held that in the backache–sciatica syndrome extra-spinal lesions could be ignored. He reminded his audience that a large-scale survey of backache–sciatica patients in the Mayo Clinic had shown that cases of disk lesions were in the minority; and he quoted with approval the opinion of Love that the disk protrusion was the commonest *intra-spinal* cause of sciatica. This meant that extra-spinal lesions were not myths.

The differential diagnosis of sciatica could be approached by the recognition of five main causes: (1) pelvic visceral disease; (2) bony lesions of the lumbar spine, pelvis, and femora—these might be inflammatory lesions or new growths; (3) lesions of the spinal, pelvic, and hip joints—in this group the protruded disk had displaced sacro-iliac strain and vertebral arthritis as the dominant lesion, though sacro-iliac strain and vertebral arthritis were still real lesions, and in his experience sciatic pain was also a common feature in osteoarthritis of the hip joint; (4) central nervous lesions proper—for example, cauda equina tumours; (5) "pseudo-sciatica," or fibrositis of the fascial, ligamentous, and muscular structures in the lumbar region, buttocks, and thighs. He believed that this type was numerically important. The condition of fibromyositis might, of course, cloak an underlying arthritic state of the lumbar spine in which degenerative changes were likely to be present in the intervertebral disks.

Posterior Crural Pain

Prof. GEOFFREY JEFFERSON, after agreeing that it was possible that the single brief attack of sciatica—how much better a name was the late George Riddoch's non-committal "posterior crural pain"—could conceivably be due to neuritis, said that it was impossible to prove it. A small disk rupture might have taken place even then. As for neuritis, it had proved too successful a diagnostic name. He thought that true neuritis in the proper inflammatory sense was a rare disease. With Mr. Kessel he had conducted a follow-up study of patients with sciatic "neuritis" seen earlier than five years ago. The unoperated series was small and replies were obtained from 26 patients. Of these two-thirds had continued to have attacks; three had been badly handicapped, and in the remainder the attacks had been of the remitting type with severe episodes only rarely.

This finding was in line with the Scandinavian reviews of close on 500 patients and lent little support to the contention that sciatica was commonly a transient and unimportant disorder. Yprehus (1947) found only 33.8% of unoperated cases able to do full work, while in Boysen's survey in 1947 only 21.1% were quite free from pain. Relapses in unoperated cases could be accounted for in three ways: (*a*) because there was from time to time a sudden further small protrusion of disk tissue; (*b*) because, the prolapse remaining unchanged, there were recurrent episodes of oedema or congestion; and (*c*) the tension caused by the hernia was intermittent because the disk popped in and out—a process he found very difficult to believe. He thought that the hernia caused pain by tension rather than by pressure on the nerve-root.

No disk protrusion had been found in only 8 out of 130 cases operated upon by himself or his assistants. The problem of alternative causes of sciatica was not as great as some suggested; nevertheless, the negative cases were important. Sufficient time had not yet elapsed for a clear picture to be formed of the after-histories of the patients with negative findings at operation. Patients from whom a disk had been removed were in the main either cured or had insignificant pain. This was so in 82% of his own series. Surgeons must agree that any operation that produced results of that order was a good operation, for none was known in any region of the body or for any condition that gave 100% of cures. The relationship between disk herniation and sciatica was now firmly established, but the history and clinical signs of both positive and negative groups were often identical. We needed to discover the differences between the two groups which should be there.

MEDICAL ASPECTS OF CHILD GUIDANCE

At a meeting of the Devon and Exeter Medico-Chirurgical Society at the Royal Devon and Exeter Hospital on April 15 Dr. HARDY S. GAUSSEN talked about some medical aspects of child guidance.

Dr. Gaussen said the child-guidance clinic was designed to deal with children in real difficulties. Studies of behaviour showed that children differed mentally from adults. The child's mind was still malleable and amenable to treatment where the adult's was rigid. The aim of treatment was to enable the child to achieve mental maturity. To bring this about it might be necessary to influence the environment, especially the parents, bearing in mind that when there was a conflict of ideas between parents and children the child was usually right. Common sense was not enough in child guidance. Team work was necessary, and the team consisted of the psychiatrist, the psychologist, and the social worker, other specialists such as the paediatrician and the special therapist being co-opted when necessary.

The approach to the problem was threefold: medical, educational, and social. Children were referred to the clinic by parents, schools, courts, and family doctors. Children who suffered from tantrums, screaming fits, sleep disorders, or who lied or were solitary, overactive, or aggressive, were problems to parents and teachers. Sick children—those with functional pain due to fears, with enuresis, with vomiting or anorexia, and with unexplained pyrexia—formed another group. A third group might be described as "magistrates' cases." Sometimes, but by no means always, these could be cured by a good beating. In Dr. Gaussen's opinion approved schools were not the complete answer; they got hold of the children too late in life. Those children in whom emotional difficulties caused diversion of energy and consequent backwardness at school were educational problems.

The whole team of a child-guidance clinic should examine each child. Physical disorders having been ruled out, the correct procedure was as follows: first, the social worker should visit the home to get as full a picture as possible of the child's background; secondly, the psychologist, usually a non-medical woman with a degree in psychology, should estimate the child's intelligence; lastly, the psychiatrist should get to know the child in a series of friendly talks, playing games perhaps, but asking no direct questions. The evidence should then be pooled and treatment planned. The combined investigation might reveal insecurity of various kinds—in relation to parents, to brothers or sisters, to being the odd man out at school, or to developmental conflicts. It might reveal educational difficulties due to a degree of intelligence superior or inferior to the rest of the class or to defects of vision or hearing or to left-handedness. It might reveal constitutional difficulties due to epilepsy or to spastic paralysis with concomitant mental defects, some of which cases inevitably ended in mental hospitals.

All these cases needed help from the child-guidance clinic. What could be done for them? Where possible, the cause must be found and treated. The parents must be guided. Social factors must be considered. It might be necessary to get the father a job, or get the school to change the child's class, or interview the schoolmaster and enlist his help in getting the child away from the mother's apron-strings. Methods of treatment might sometimes be applied with advantage to groups of children. In some cases institutional, and in others individual, treatment was the method of choice.

ALLERGIC CONDITIONS OF THE EYE

The second general meeting of the British Association of Allergists was held at Oxford on April 17. A discussion on allergic conditions of the eye was opened by Dr. VERA B. WALKER, who gave an account of her experiences during seven years' work. Dr. Walker presented some of her results obtained with specific desensitization, comparing them with those following non-specific desensitization with histamine-azo-globulin; where the specific allergen could not be determined desensitization with histamine provided an alternative line of treatment. Dr. Walker made special reference to three conditions—conjunctivitis, keratitis rosacea, and migraine. She emphasized the urgency of referring all cases of keratitis rosacea to the allergists for investigation, and indeed other patients with keratitis of unknown origin, especially those with a family history of acne, eczema, or urticaria.

Discussing the treatment of allergic migraine, Dr. Walker drew particular attention to the significance of a low systolic pressure. Although all cases of migraine were not of allergic origin, if a patient with true migraine had a low systolic pressure, then allergy should be suspected and treated appropriately.

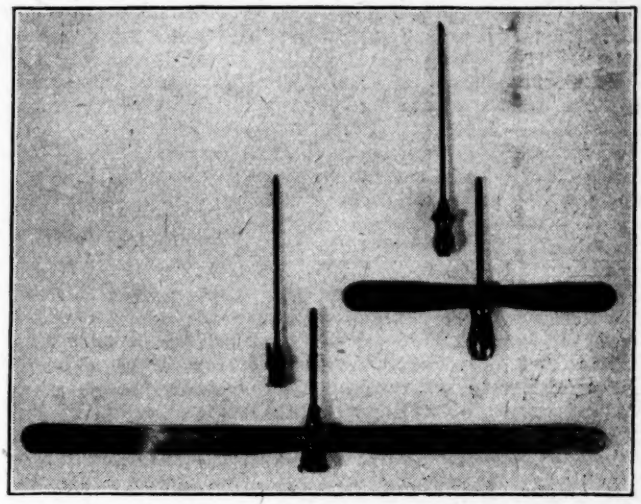
The subject was then thrown open to discussion and Mr. FREDERICK RIDLEY, Mr. A. C. HOULTON, Mr. ANTHONY PALIN, and Dr. R. S. MACLATCHY contributed observations from the point of view of the ophthalmologist. Other speakers included Dr. A. W. SPENCE, Mr. DRUMMOND CURRIE, Dr. R. W. STEPHENSON, Dr. C. J. C. BRITTON, Dr. LIPMAN COHEN, Mr. VICTOR PURVIS, Dr. F. WRIGLEY, and Dr. D. HARKINS.

Preparations and Appliances

TRANSFUSION NEEDLE FOR INTRAVENOUS CANNULIZATION

Dr. J. H. WAELSCH, of the Central Laboratory, Bulovka Hospital, Prague VIII, writes: In carrying out transfusions, especially those repeated at short intervals, it is necessary to prevent damage to skin and veins which might arise from repeated insertions. The normal needles supplied with the various types of apparatus for drip transfusion allow direct piercing of the vein and skin, and have the disadvantage of leaving a sharp point in the vein, which not only endangers the vein by perforation but also irritates its walls and may cause the formation of small blood clots. Also, contact of the point of the needle with the walls of the vein may slow down or entirely stop the transfusion. On the other hand, the introduction of a cannula damages the skin, even though the damage is slight. The place used is thus rendered unsuitable for transfusions at short intervals. This seems to be the case when using the method described by A. Clain (*Lancet*, 1947, **2**, 830), who makes a short skin incision with a scalpel.

The type of transfusion instrument for intravenous cannulization described below, which we used for more than a year, makes it possible to pierce the skin as with the ordinary transfusion needle. It combines all the advantages of transfusion



by blunt cannula without necessitating the use of a scalpel, so that injections can again be made on the same spot within a very short time. It consists of the transfusion cannula, to which wings are attached, and an injection needle which is enclosed by the cannula. The illustration shows two types of the instruments, which are made in three sizes.

The injection needle fits tightly into the cannula whilst allowing of its being moved to and fro. The needle-tip lies immediately in front of the blunt tip of the cannula, so that no unevenness is felt by the patient when the skin is pierced. The mount of the needle and cannula can be attached to "Record" syringes. The mount of the needle is provided with a tooth to fit into a notch made in the base of the cannula to prevent independent rotation of needle and cannula. If no metal adapter is available the tubing of the intravenous apparatus can be attached simply by being pulled over the olive mount of the cannula. Wings made of flexible metal with a roughened surface are fixed to the cannula.

Procedure.—Insert needle into cannula so that the tooth on the needle falls into the groove on the cannula, and attach syringe. Clean the skin of the patient and apply compression in the usual way. Pierce skin and insert the instrument into the vein. When it has been ascertained that the instrument is in the vein, release compression and withdraw the needle, leaving the cannula in the vein. It is essential that the instrument be inserted into the vein far enough, so that the cannula is still well in the vein when the needle has been withdrawn. The intravenous apparatus, which is set up in the usual way, is then attached to the mount of the cannula by an adapter or by the rubber tubing being pulled over the olive. The wings of the cannula, which can be shaped to the form of the limb, are then fixed with "elastoplast." When the transfusion is finished the cannula is withdrawn and the skin treated as after intravenous injections.

The needles were made for me by F. Špirk, instrument makers, Prague XVI, Hlubočepy 399, and can now be manufactured by Willen Bros. Limited, Surgeons' Instrument Makers, 44, New Cavendish Street, London, W.1.

In recognition of his doctor's "kindness, understanding, and devotion to duty" a Mr. J. L. Street, of Dewsbury, who died on March 31, has bequeathed his body to the doctor or his successor for medical research, reports the *Yorkshire Post*. The doctor concerned died last October himself and his successor has therefore accepted the bequest and given the body to Leeds Medical School.

Correspondence

Control of Regulations

SIR,—It appears that, while Mr. Bevan's recent promises have not satisfied many of the doctors, there is an even larger section of the profession which wishes to be rid of this controversy. The monster about to be born seems capable of creating great misery. Since we do not possess the power of superfecundation, all we can hope to do is to palliate the Minister's evil potentialities.

To the specialist, whose terms of service are to be determined by Regulation, a satisfactory check on Regulations would seem essential and sufficient. For the general practitioner there appears to be no public support for the retention of buying and selling of practices. The system of payment by capitation fee will exert an economic negative direction which will not be removed by annulment of the negative-direction order. Thus the only means of preserving his freedom is the same as for the specialist.

If there is still a vote for abstinence from the Health Service Act as it is to stand, a compromise proposal from the doctors would have considerable public support and be successful. In such circumstances I suggest a memorandum on the following lines: (1) The B.M.A. reaffirms its desire for a comprehensive health service. (2) If the Government will insert in the Amending Act a provision that the Regulations under the National Health Service Act, 1946, shall be subject to the provisions of Sect. 1 of the Rules Publications Act, 1893 (or a suitable modification thereof), and that the B.M.A. and Royal Colleges shall be considered as public bodies under this Act, then, notwithstanding the many and varied other objections to the Act, the B.M.A. will recommend the doctors to accept its provisions and work for its improvement. Better to have a solution on these lines than a fight in which all will suffer.—I am, etc.,

London, N.W.11. HAROLD E. THOMAS.

Comprehensive Service

SIR,—In common with many others I am at a complete loss to understand the policy of the B.M.A. in regard to the Health Act. Do they want the Act or do they not? Your leading article in the *Journal* of April 24 (p. 791) and Dr. Dain's letter (p. 805) seem to add to the confusion. Lord Horder's letter to the *Daily Telegraph* seemed almost to be an apology for Dr. Dain's speech, but at least it gave a clear view of the situation that will arise if the profession compromises on any of the B.M.A. four points.

I submit that even if all four points are conceded by the Minister we shall still be acting dishonestly to the public if we agree to participate in working the Act as from July 5. We know the facts about shortage of hospital beds, equipment, nurses, etc. We know that our middle-class patients will be particularly hit by the cost of the *compulsory* State insurance scheme and that the most of them will have to pay in addition for private ward or nursing-home in the absence of the promised free hospital bed. The present insured population will suffer greater hardship by this added competition for the available beds. We made no election promises nor did we distribute rose-tinted spectacles in 1945. Why should we now make ourselves the scapegoat of the politicians of all parties who blessed the Beveridge Plan?

I submit that the B.M.A. is wrong in reiterating that we all desire a comprehensive medical service, if by that they mean a service which is a necessary corollary of the Beveridge Plan and a service to which subscription by everyone is compulsory. The only comprehensive medical service to which I myself will agree is one which is open to everyone but to which everyone is free to subscribe or not. At least those who wish should have the right to contract out before we touch the Act.

It is self-delusion to think that we can retain professional freedom by a process of give and take over four subsidiary and debatable points, if we have sold the pass and let it be understood that with some modifications we will agree to work a compulsory scheme. Add direction in sickness to direction of labour, plus compulsory State medical records of everyone, and you have the complete Nazi system in embryo thrust upon us. We cannot claim freedom for ourselves and at the same time become the agents of any Government, of any party or coalition, in binding a totalitarian system on the whole nation. To think such possible is a confession of a disordered mind. If we agree to work an all-in compulsory scheme like the Health Act, we shall sell out to Communism. I have voted "No," and mean to vote "No" as consistently as Molotov.

If the B.M.A. cannot act on the clear expression of the profession's opinion in the last plebiscite and leave the Minister to stew, to carry out his boast that he will work the Act with or without the doctors, and if in spite of this they must go running around to him for conversations, then the melancholy thought arises: Are there in high places in our Council some who really want this totalitarian Act to come into operation for personal reasons? If this be so, then for all time their honour will stand rooted in dishonour, for they will have manœuvred the free medical profession into becoming agents of tyranny.

Our ancestors fought and died for religious and civic freedom, and for myself I will never take part in thrusting the delusion of complete social security (whether supported in the name of Beveridge by Conservative or Socialist or Liberal Party) upon my fellow citizens. As students of biology we ought to know that we live in a competitive world where survival is only possible by individual effort. Our hospital system with all its human shortcomings is the visible expression of the Christian faith of our fathers. To hand them over to the State and to make them dependent on forced subscriptions is to admit that the compulsion of the Christian ethic no longer acts on our conscience.

It is a fact that nearly all thinking citizens are now looking to us as their last hope of freedom in our time. If we fail to stand fast then it will be for all time to our discredit as a profession. We blamed the Germans for not protesting at the risk of their lives against Nazism in its early days. The same choice is now before us as a profession, but with no comparable risks, if we refuse to become agents in binding our country with chains of tyranny.—I am, etc.,

Bournemouth. DAVID HARDIE.

SIR,—You say in the *Journal* of April 17 (p. 737) that the profession is committed to a comprehensive medical service. This was a colossal and fundamental mistake and it is recognized as such now by the immense majority of the profession. Is it right that any profession or body of men should be tied to such a mistake made by their leaders? I am quite sure that if Mr. Aneurin Bevan found a mistake like that in his Act he would have an Amending Bill introduced into the House the next day. Let the Council take a plebiscite on the 100% policy and see what the result would be.—I am, etc.,

London, W.5. J. B. MASON.

The Minister's Gesture

SIR,—While heartily welcoming the Minister's gesture and particularly the tone in which he spoke, I am afraid I see no great cause for rejoicing, nor for another plebiscite. After all, it is only a step—a small step, I feel—towards solving the problems confronting us. Apart from three rather minor concessions which are to be incorporated in the Act, the rest of our road seems paved only with good intentions couched in vague terms: "Not in *prospect*" (Question 3); "ought . . . to be ready to indicate its *likely attitude*" (Question 3); "appointed *after consultation* within" (Question 4); "will be *asked* to observe the wishes of" (Question 11a); "would be *taken into account* by" (Question 11d); etc. Not really very reassuring, I fear.

In the three "concessions" he is merely (1) incorporating in an amending Act an assurance he himself had already given (*Hansard*, Nov. 4, 1946, Vol. 428, C. 1125) ensuring that a full-time salaried service can only be instituted after a further Act of Parliament. (Is putting in writing what has already been promised verbally really a concession?) (2) Amending (if need be) the Act relating to partnership agreements, which was so ambiguous that grave injustices might have occurred. (Is amending an Act so worded that its meaning was ambiguous and liable to cause injustice really a concession?) (3) Juggling

with the strings attached to the unhappy basic salary. But the salary remains—a noxious thing. Obviously there must be something given for that £300 or the Treasury would veto a waste of public funds. Direction, or negative direction, seems indicated.

Freedom of speech and publication, though again assured verbally by the present Minister, are still not to be incorporated in the Act and so made binding on his successors. Ownership of goodwill, which would solve so many other problems (and make "concessions" Nos. 2 and 3 unnecessary) and for which no detailed, equitable, workable alternative has yet been put forward, has not yet been conceded. The powers of the "unofficial G.M.C." to prevent a qualified practitioner doing midwifery under N.H.S. remain. There is still no right of appeal to the courts, and the powers of the Minister remain such that he might well be renamed the Dictator of Health. We have stated what we consider essential for a satisfactory Health Service and have conceded all else. Now it seems to be suggested that as Mr. Bevan has made a gesture we should concede the rest.—I am, etc.,

Rugby. R. PRESTON HENDRY.

Established and New Practitioners

SIR,—Mr. Bevan wishes to abolish the buying and selling of practices so that the young doctor shall start practice without financial difficulty. Many doctors agree, but it seems unfair at the institution of such an innovation, if proved a wise one, that practitioners already established and yet still treading the fires of financial stress should be penalized.

In the new Health Service a change for the better is to take place for the young doctor about to commence general practice. None is so conservative as to object to innovation to improve conditions for the next generation, but let it not be at the expense of those men in established practice who have in most cases already paid large sums of money in capital outlay, and subsequent sums to purchase additional shares and/or pay out a senior partner.

May I suggest that as at July 4, 1948, a line should be drawn between the old and the new, and that all doctors in established practice, whose names appear in the *Medical Register* and who have for so many years served the public faithfully and well, should be compensated adequately both for capital outlay *and* subsequent payments they have had to make while building a practice. More important, still, that fair compensation should be paid to them, if they so desire, within a definite stated number of years (say, five)—those fortunate enough not to require their money immediately to be paid, as already suggested, at death or retirement.

The above suggestions are of little concern to the young man not yet embarked on G.P., nor to the doctor long enough established to have saved for retirement or old age. They do most apply to the main body representing general practice—doctors of ten years' standing or so—who have to meet the heaviest financial commitments of a busy practice and a young family. It is the vote of this group of practitioners which carries most weight in any plebiscite for or against a National Health Service.

Surely if these debatable points were concisely and quickly clarified, and the probability of realizing the capital value of a practice *within a specified number of years* was certain, there would be less apprehension for one's future financial stability, and with a mind composed each doctor would be better able to reconsider his decision for or against service in a national health scheme.—I am, etc.,

Birmingham. G. A. POWELL-TUCK.

More Safeguards

SIR,—I am among the majority who desire to continue to refuse service under the N.H.S. until there is sufficient safeguard of the freedom of the profession. So far as general practitioners are concerned, for an eventual 100% Government service I am convinced that there are three essential safeguards of our security which have not to my knowledge so far featured in such negotiations as have taken place. They are :

(1) Complete removal of the power of dismissal from the Service from the hands of the Minister and of any committee under his jurisdiction. Dismissal should be in the hands of the General Medical Council, as it is equivalent to removal from the *Register*, and should be allowable on ethical grounds only—i.e., for neglect of patients and not for neglect of regulations. Breaches of important regulations could be dealt with, if considered necessary, by other means such as fines.

(2) Inclusion in the Act of the scale of remuneration in general terms—e.g., that it shall be in accordance with the recommendations of the Spens Committee. Details of its interpretation may then be subject to negotiation between the Minister and the profession.

(3) Inclusion in the Act of the recognition of the British Medical Association as the authorized negotiating body for general practitioners. If this is not included the Government may at any time after our acceptance of service rule that collective action by the B.M.A. is illegal, since it is not a trade union.

Whatever the outcome of negotiations about retention of goodwill, negative direction, etc., I believe these three practical points to be fundamental to our security after the Service has been joined.—I am, etc.,

Hove, Sussex. E. N. G. GORMAN.

Alternative Service

SIR,—I believe that this latest plebiscite will show a smaller all-round vote and a smaller number of outright rejections of the Service because many of us feel that the "Molotov" attitude is not enough, that the B.M.A. should be telling the Government and the public, especially the latter, what we will do rather than merely what we will not. If my forecast is wrong there is no more to be said: if it is correct there is still time to modify our method of counter-attack.

While those of us who are in medicine know well enough that the new Service will make no difference to the health of the people, we must recognize that the great mass of people wish to pay for medical treatment on a contract basis. This is the essence of the new Act and ought, I believe, to be accepted by the doctors. All the points to which we have made strong objection are not essential and may justifiably be rejected.

I suggest that the profession should make a declaration to the public and to the Government along these lines : (1) We agree to run a 100% service to be paid for on a capitation basis at a rate in conformity with the Spens Committee report. (Patients preferring private attendance could still obtain it and would not necessarily lose sick pay, since private certificates would be accepted.) (2) The question of the buying and selling of goodwill, direction, etc., to be postponed for five years. If after that time it can be shown that the Service is not working effectively for lack of these elements, the Government can approach the profession afresh in respect of them.

I submit that this procedure would have the following advantages : (*a*) It would demonstrate to the public that we are not trying simply to prevent the introduction of the new Service for our own ends but are prepared to serve them adequately. (*b*) It would, I believe, be endorsed by a greater number of general practitioners than rejected the Service in the last plebiscite. I can say nothing as to the consultants, since I have no more idea than they as to what they are being offered. (*c*) Five years' participation in a national service would bring the solidarity of the profession (so much a product of this controversy) to the same level of effectiveness as the National Health Insurance Service has achieved ; and less than two years ago we had a useful demonstration of what this means in negotiations with the Government.—I am, etc.,

Northwich, Cheshire. J. BOYD FULTON.

Postpone Service

SIR,—In the beginning Mr. Bevan was briefed to take the proposed new Health Service and work it according to certain principles. In order to achieve this object he devised his battle orders in two distinct phases. The attack in phase I, in which the National Health Service Act passed into the Statute Book, was directed at the general public and Members of Parliament. Doctors' representatives were first ignored and then abused. Soon after the Bill became law phase II was put into operation and is now nearing its height. Its objective is to lure the

profession into the trap. Notice how the technique has changed. The Minister is now conciliatory and makes "considerable" concessions to this reactionary profession. There are ominous signs of weakening in the Council of the B.M.A., as reflected in the wording and tone of the last leading article (April 17, p. 737).

We have stated publicly that we will adhere to our four "freedoms," which we regard as essential for the protection of our patients and ourselves. Nothing has changed since that decision to alter the material position in any way. Mr. Bevan has done exactly as Dr. Dain forecast weeks ago. He has given way on one small point in order to force a breach in our defences. Our answer should be to close that breach with a decisive "No" to the plebiscite question.

In my view the Act's implementation should be postponed, even if there was agreement on the main clauses, until the detailed terms of service such as hours of work, secretarial assistance, and holidays have been decided. It seems to me incredible that we are being asked to sign on for a lifetime's job with no possibility of an alternative, and are told that the conditions of work will be settled "later on."

As has been stressed so often, our strength is in unity. By sticking together we can postpone this change for the worse in the medical services of this country and so easily make it a change for the better. The National Health Service Act contains so much that is good that it is a pity to pluck the fruit until it is ripe, and until the maggot has been removed from within.—I am, etc.,

Brixham, Devon KENNETH INMAN.

The Plebiscite

SIR,—I wish to record my protest against the hurried manner in which the recent plebiscite has been conducted. It seems to me entirely wrong that any medical man should be expected to make what is, or ought to be, a major decision in his life without opportunity for due consideration and discussion with his colleagues.—I am, etc.,

London, W.1 DOUGLAS ROBERTSON.

Position of Assistants

SIR,—Dr. John Gemmell's letter (April 24, p. 810) rightly stresses the unsatisfactory position of present-day assistants, both now and in the future Health Service. Nothing has emanated either from the B.M.A. Council or from the Minister to guide and encourage them. Indeed, it would appear that in the future, as in the past, their role will be the same—a source of cheap labour, liable to a month's notice at any time and *positively* directed from the area by restrictive covenants in their agreements, although, as Dr. Gemmell says, they may have built up "a certain goodwill by their own merit."

The Act at present provides that assistants will not be eligible for automatic inclusion in the list of doctors participating as principals in the new Service. An assistant, however, will be able to continue to assist any doctor permitted to have an assistant, or to secure admission to the list as a principal if the Medical Practices Committee consents. This of course means if his employer consents; for the Committee will naturally consult the principal regarding his assistant's application. The assistant therefore remains at the mercy of his principal. He can be given notice at any time without reason, and yet he may be as good a doctor as his principal, as well beloved by his patients, and as keen as ever on working in the area which he chose when he took on the job.

Dr. Guy Dain, the day after the Bill received the Royal Assent, assured me that the Minister was to be impressed that restrictive clauses in assistantship agreements must continue. The Minister has agreed to this apparently, for there is nothing in the Act as it now stands which precludes such clauses from operating after July 5. In doing so he has in my opinion given principals a protection to which they are not entitled in law (it is one of the concessions he has made to the B.M.A., although we hear little of it) for this reason:

During the hearing of the case *Routh and Wilson v. Jones* before Lord (then Mr.) Justice Evershed, and later before the Court of Appeal (*Journal*, May 17, 1947, p. 700), it was established that a principal can only be protected in law from competition by a previous assistant in so far as the knowledge which the assistant has gained of the practice and of the patients of the practice may adversely affect the selling value of that practice. The Health Act provides full compensation for the selling value of the practice of a principal entering the Service. Why, then, should the principal be still further protected from competition by a previous assistant? There is no protection in law against free competition, and the B.M.A. indeed insists that it is essential to ensure good work.

If the present status of the assistant is allowed to continue it means that his income will be restricted to the present rate of pay while the principal reaps the financial advantage of an extra 2,400 capitation fees. I would therefore support Dr. Gemmell (and the other writers whose letters have appeared at infrequent intervals without stimulating any official reply) in asking that the position of present-day assistants be classified. There are many with first-rate experience who, because of their war service and the financial loss they have in consequence suffered, find themselves forced to take assistantships in order to provide for their families. Some of them, principals before the war, lost their practices and in some cases their property too. They cannot afford to buy practices, houses, and equipment at to-day's prices. They are, I believe, entitled to more consideration from the B.M.A. Council and from the Minister than they have so far received. They are also entitled to a measure of representation.

There is no reason, if B.M.A. principles are sincere and apply to all members of the profession, why any assistant in the future Service should be prevented from practising as a principal in the area in which he has served as an assistant.—I am, etc.,

Okehampton, Devon C. G. JONES.

Bewildered Practitioners

SIR,—On demobilization after the recent major conflict I was vaguely surprised that the B.M.A. took so little notice of the "returning doctor." However, I comforted myself with the thought that the entire organization was probably concerned with working out operational orders for "Operation Bevan." Since that day I have listened to a vast quantity of irrelevant ideas propounded by elderly practitioners whose lack of understanding of the problems of the young ex-Service doctor is only surpassed by that of the Royal Colleges when it comes to general practice.

While we talk and negotiate and vote the sands are running out, and on July 5 a herd of bewildered practitioners will join the Service because nobody has told them what to do if they stay out. So let us have some clear-cut directives from the trustees of the Independence Fund, and let us have them at once, so that local schemes can be worked out ready for the appointed day.—I am, etc.,

St. Neots, Hunts. IAN H. BARCLAY.

N.H.S. Capitation Fee

SIR,—It seems to have escaped general notice that the capitation fee of 18s. which we shall receive under the new Health Act (it will be less in most cases after the first charges have been deducted from the pool of £41,000,000) falls short of the figure, translated into 1948 values, recommended by the Spens Committee Report by more than 5s. per head. The Government promised to implement the Spens Committee recommendations. How some of us appear to be fooled about this, as well as about the infinitely more important issues of our professional freedom and fundamental civil rights, is beyond comprehension.—I am, etc.,

Salisbury. PAUL HARRIS.

Statement to Patients

SIR,—At a meeting of local doctors the following statement, for display in waiting-rooms on and after April 5, 1948, was signed by 24 out of 25 doctors engaged in general practice in the area.

We, the undersigned medical practitioners, practising in the Harefield, Ickenham, Hillingdon, Uxbridge, Yiewsley, and West Drayton Areas, while welcoming a Health Service suitable for the whole community, consider that the National Health Service Act of 1946-7 as at present enacted would be detrimental to the welfare of our patients and the proper practice of medicine. For these reasons WE HEREBY GIVE NOTICE to our patients that in accordance with our rights under the said Act, we will not enter into any statutory contracts of service as provided for in the said Acts IN THEIR PRESENT FORM.

—I am, etc.,

R. A. G. HAMILTON,
Local Hon. Secretary.

Uxbridge, Middlesex.

Freedom not to Treat

SIR,—During the past months a great deal has been said about the undesirability of central control of treatment, but I wonder if anyone can help me to solve this type of problem. Take a recent experience of mine: I am consulted about a young woman whom I find to be a fairly florid schizophrenic unsuitable for admission to my general hospital. The relevant county mental hospital does no insulin treatment on the female side. The neighbouring county mental hospital does but cannot undertake treatment of "non-domiciled" persons. The nearest city mental hospital can do so but does not do insulin treatment on the female side owing to shortage of staff—and so on over an area of several thousand square miles. An application to an L.C.C. mental hospital for assistance draws advice to get her admitted locally or wait until July 5.

For about half of the modern "psychopathological" period insulin has been recognized as the weapon of choice for this illness, and to-day, 13 years after 1935, I cannot get this girl treated even as an act of grace.—I am, etc.,

Norwich. R. LOUIS ROSE.

Acute Intussusception in Childhood

SIR,—In their interesting discussion of the diagnosis of intussusception in infancy (April 24, p. 776) Drs. Brenda Morrison and Donald Court make no mention of a finding which seems to me perhaps the most helpful and significant of all. On making a rectal examination, when the finger is withdrawn, in intussusception and in intussusception alone there is absolutely no faecal odour upon the finger-stall, even when it is smeared with mucus and blood. In all enteral infections, on the other hand, the odour is always strongly faecal.

One other point seems to me important, because it is apt to convey a deceptive reassurance. For long, in the intervals between the pains, the baby commonly falls asleep and may present all the appearance of normal, peaceful health, so that for anyone not familiar with the condition it is difficult to believe that the danger is so urgent.—I am, etc.,

London, W.1. HECTOR CHARLES CAMERON.

Iron-deficiency Anaemia in Pregnancy

SIR,—I was interested to read the article by Prof. L. S. P. Davidson and Dr. R. H. Girdwood (April 17, p. 733) on the subject of the treatment of refractory iron-deficiency anaemias with intravenous iron. Although engaged wholly in general practice, with its limited but frequently underestimated opportunities for clinical investigation compared with the facilities offered in hospital, I have for some time taken considerable interest in the treatment of iron-deficiency anaemia in pregnancy.

From about the sixth month of pregnancy onwards the foetal demands increase rapidly, and when the physiological anaemia of pregnancy has been excluded and a true iron deficiency exists, oral iron therapy has been found to have several disadvantages:

1. An appreciable number of cases show intolerance to iron administered by the oral route, and symptoms of alimentary irritation such as flatulence, nausea, anorexia, and diarrhoea make adequate dosage impossible.
2. In those cases in which symptoms of intolerance are not so prominent, unsatisfactory increase in the haemoglobin level is frequently observed. This is probably associated with the hypochlorhydria or achlorhydria which is a more common finding at this stage of pregnancy.
3. It is most desirable to ensure maximal haemoglobin levels and adequate iron storage at the time of parturition, but time may be too short to achieve this by oral therapy.

I feel, therefore, that any form of therapy would be most valuable which would tend to ensure maximal haematological response, and which would not be influenced by those factors already mentioned which interfere with the absorption of iron from the gut and with its subsequent utilization in haemoglobin synthesis.

When Nissim's paper appeared, on the use of intravenous iron in hypochromic anaemia (*Lancet*, 1947, **2**, 49), I felt that a safe and effective preparation of this type might be of definite assistance in my own investigations. It appeared, however, that the method of preparing solutions of saccharated oxide of iron was not at that time sufficiently reliable to ensure the production of similar batches of material, at all times free from toxicity, with standard therapeutic effectiveness after efficient sterilization. This difficulty has been stressed in Prof. Davidson's recent paper (April 17, p. 733), but some months ago I was able to obtain a solution of saccharated oxide of iron (containing 2% of iron) which is evidently prepared by a process fulfilling the requirements mentioned.

I have carried out investigations with this preparation on a series of cases, both at different stages of pregnancy and during the puerperium. The majority of the cases were ambulatory, and no difficulties have occurred during treatment. During this investigation considerably more than one hundred 5-ml. and 10-ml. injections of this preparation have already been administered in a period of over three months, and I agree with the statement made by Slack and Wilkinson (April 17, p. 753) that the injections present no special difficulties after the simple technique has been acquired, and no elaborate precautions have to be taken other than gradual dosage increase and slow administration.

This investigation is proceeding and detailed clinical results will be described later, but I can state that my preliminary observations show a dramatic response to this treatment when a true iron deficiency exists. The absence of the symptoms of intolerance associated with oral iron administration already mentioned and a satisfactory rise in the haemoglobin percentage enhance the feeling of well-being and contribute substantially to the patient's confidence and co-operation.

I have found that intravenous iron therapy administered before parturition ensures adequate iron reserves in the body in addition to correcting the anaemia. As a result, satisfactory haemoglobin levels have been effectively maintained after parturition without further need for iron by any route.—I am, etc.,

Kidsgrove, Staffs. D. G. FRENCH.

Iron in Anaemia

SIR,—With reference to the question and answer on iron in anaemia (March 27, p. 625), it is suggested that ferrous iron is rapidly converted to the ferric state in the patient with achlorhydria but that there is little clinical evidence in support of this. I have observed anaemia to follow gastrectomy and have also noted that giving iron by the mouth is sometimes ineffective as a cure. Two obstinate cases were cured by giving to one extra milk and intramuscular calcium, and to the other intramuscular calcium alone.

The latter is a woman of 50 who was seen a year after gastrectomy with Hb 58%, brittle finger-nails, falling thin hair. Neither iron nor calcium by the mouth was tolerated, so intramuscular calcium with vitamin D was given on alternate days for six weeks. The Hb rose to 92%, the hair and nails soon began to recover, and she regained her lost energy. This sequence of events has been repeated twice.

The question arises as to whether a lack of calcium can cause an inability to absorb iron, or whether calcium can under some circumstances "save" iron, or whether the improvement in nutrition caused by the calcium and vitamin D was responsible for the better absorption of iron. It has been noted that general improvement in diet improves the Hb in the circulatory blood, and that is perhaps why Hb estimations in expectant mothers in this country to-day are higher than before the war, for their diets to-day contain certainly no more iron but equally certainly more milk.—I am, etc.,

Leeds, 7. R. A. MURRAY SCOTT.

Lupus and Cod-liver Oil

SIR,—Dr. G. B. Dowling *et al.* (March 6, p. 430), quoting a recent American article, state that Emery in 1848 first described the treatment of lupus with massive doses of cod-liver oil. This is incorrect. Devergie's original paper (*J. Méd. Chir. prat.*, 1848, **19**, 411) on this subject appeared in May, that of Emery in September (*Rev. méd.-chir. Paris*, September, 1848). Devergie states that he had used cod-liver oil—the most fishy "l'huile brune" variety—as well as other treatments for eight years, and that "aulourd'hui je n'hésite pas à déclarer que c'est de tous le plus efficace: je vais plus loin, et j'avance qu'administré suel il guérit. Cette assertion est tellement vraie, qu'à partir du moment où ce moyen a été mis en usage par quelques-unes de

nos malades, les autres m'ont successivement prié de le leur faire prendre." The dose was "une cuillerée à bouche" night and morning, which was increased every two or three days by another tablespoonful, until about three were being taken at one time. When once this dose was reached most patients ceased to dislike the oil, so that it could be rapidly increased to the desired maximum of 12 to 14 tablespoonfuls daily. Treatment had to be continued for three to six months or even longer. The appetite of the patients decreased but their weight and general well-being increased.

Emery's original paper is not listed as being available in any library. The American reference to it is really a reference to an abstract—an abstract which was apparently inaccurate in 1848 (*Bull. gén. Thér. Paris*, 1848, **45**, 466) and which in its turn has been inaccurately summarized in 1947 (*J. Lancet*, April, 1947, p. 152). Indeed it appears to be impossible to know now what Emery really wrote, let alone what he really did; but it seems incredible that his patients drank 1,000 g. (nearly 2 pints) of cod-liver oil daily, while the 12 to 14 tablespoons (about one-third of a pint) of Devergie are at least possible. Can it be that Emery was the result of a juvenile frolic of Karl Friedrich Hieronymus, Baron von Münchhausen (1720–1797)?—I am, etc.,

London, W.1. FRANKLIN BICKNELL.

Papworth Village Settlement

SIR,—When the Disabled Persons (Employment) Bill became law it was apparent to workers in the tuberculosis field that the facilities for training and employment provided therein, while suitable for the ordinary disabled person, were hardly possible of application to the man and woman disabled by tuberculosis. For some time past negotiations have been going on between Papworth Village Settlement and the Ministry of Labour to provide some scheme for training which would be of assistance to tuberculosis sufferers. The Ministry of Labour has now agreed to recognize as vocational trainees all trainees (other than Ministry of Pensions cases) at Papworth who are able to work for a minimum of three hours a day. This recognition will extend to those who have completed their sanatorium treatment elsewhere as well as to patients who have received their sanatorium treatment at Papworth.

The following terms have been agreed:

(1) Training allowances will be paid to all recognized trainees on the scale set out below; sickness benefit will not be payable.

(2) The Ministry will pay hostel charges in respect of each recognized trainee at the rate of 28s. per week for men and 22s. 9d. per week for women.

(3) No training grants will be paid to the Settlement by the Ministry.

(4) The period during which the Ministry will pay training allowances will depend on the trainee's progress. It is understood that the average period is likely to be well under two years. In no cases will allowances be paid for more than three years.

(5) When a trainee has finished training he will be considered for colonization in the Settlement at the trade union rate.

(6) Quarterly reports will be rendered to the Ministry of Labour, and, where it appears that the trainee is unduly prolonging the period of training or otherwise proves that he or she is unlikely to benefit from further training, the Settlement will advise the Ministry to terminate training. Reports will also be rendered if so desired to the local authority responsible for treatment.

TABLE I.—*Persons Aged 20 and Over*

Rate	Amount per Week	
	Men	Women
A	35s.	28s.
B	40s.	33s.
C	45s.	38s.
D	50s.	43s.

Rate A applies to persons without dependants. Rate B applies to persons with one or more dependent children under 16 but with no adult dependants. Rate C applies to a married man with wife or in certain circumstances a man or woman with an adult dependant other than a wife. Rate D applies to a married man with wife and one or more dependent children under 16, or in certain circumstances a man or woman with an adult dependant other than a wife and one or more dependent children.

TABLE II.—*Persons under 20 Years of Age*

Age	Amount per Week	
	Young Men	Young Women
19	26s. 6d.	24s.
18	23s. 6d.	23s.
17	22s.	21s.
16	22s.	21s.

The allowances are payable without regard to any payments received from the Service departments during paid furlough or to any disability pension or similar allowance (excepting those cases already excluded from the scheme—i.e., Ministry of Pensions treatment allowance cases).

Persons who leave home for training will receive, in addition to the appropriate rate of allowances, full board and lodging free of charge. A person in training away from his home area who continues to maintain his former home may receive additionally an allowance of 24s. 6d. a week.

Married men under 20 years of age, and in certain circumstances unmarried men aged 19 and women aged 19 who have dependants, receive allowances at rate (B) or (C) or (D) above, as appropriate.

Other persons under 20 years of age who have dependants receive 10s. for an adult dependant and 5s. for a dependent child under 16 in addition to the allowances set out in Table II.

During periods of sickness of a week or more training allowances will not be paid. Sickness benefit and training allowances will not be paid concurrently.

This scheme will now enable local authorities to send selected cases to Papworth at less cost than hitherto, as part of the cost of maintenance will be borne by the Ministry of Labour (see (2) above). The decision as to suitability for admission to Papworth and the scheme will rest entirely with the medical staff at Papworth, who will require full clinical details and *x*-ray films in each case from the tuberculosis officer.

Both the Committee of Management of Papworth Village Settlement and the Ministry of Labour feel that this is a considerable step forward in the rehabilitation of the tuberculous, and anticipate its extension in the future. To this end the Ministry has undertaken to provide half the cost of two hostels of 50 beds each for men and women at Papworth.—I am, etc.,

Papworth Hall, Cambridge. RICHARD R. TRAIL, Medical Director.

Thiosulphate as an Aid to Chemotherapy

SIR,—A recent report by Lorant[1] on the subject of the non-specific chemotherapy of malaria by thiosulphate has given us a great satisfaction, for during the war we carried out experiments from a similar view-point and obtained similar results.[2] We had previously confirmed the fact that thiosulphate, in spite of its being a single inorganic substance of a simple chemical constitution, acts in various cases (lewisite, mustard gas, cyanide, and carbon monoxide poisoning) like a "universal detoxifier" (Kabelik[3]), and this may probably be ascribed to the following factors: (1) Thiosulphate as the neutral salt of thiosulphuric acid behaves like an inorganic glutathione, combining with certain toxic agents and rendering them practically non-toxic. (2) Being oxidatively converted to sulphuric acid, thiosulphate supplies an abundant exogenous source of ethereal sulphates. (3) Thiosulphate intensifies the biological defence reactions by activating the reticulo-endothelial system.

In addition to the detoxifying actions as above mentioned, thiosulphate possesses an activating effect on certain chemotherapeutic agents, particularly neoarsphenamine in syphilis and "optochin" in serpiginous ulcer of the cornea. In both cases thiosulphate not merely elevates the tolerance of the organism for those agents, but also seems to increase more or less markedly their bactericidal effect.

Suggested by these inferences, we undertook a few experiments on birds concerning the effect of combination of thiosulphate with quinine in comparison to the routine treatment with quinine alone. Canaries were inoculated with *P. praecox*, and three days after this they were divided into three random groups and subjected to the following procedures:

1. Quinine and thiosulphate group. The birds were injected daily with 0.2 ml. of 2% calcium thiosulphate solution (corresponding to the confirmed optimal dose of about 0.2 g. per kg.

body weight) and one hour later with 0.2 ml. of 0.5% quinine hydrochloride solution.

2. Quinine group. The birds were injected daily with 0.2 ml. of physiological saline solution and one hour later with 0.2 ml. of 0.5% quinine hydrochloride.

In both groups the injections were given intramuscularly and repeated for four consecutive days.

3. Untreated control group.

From the fourth day of inoculation parasites were examined almost daily microscopically by Giemsa's method. The intensity of their development was estimated by counting them in a given number of fields.

On an average, the degree of development of parasites on the 12th day in the quinine-thiosulphate group corresponded approximately to that of the 9th day of the quinine group, and it can be said that in the experimental conditions thiosulphate brought about an inhibition equivalent to about three days. This result may be attributable, apart from the three factors already mentioned, to some degenerative changes in the protoplasmic constitution of the microbes caused by direct action of thiosulphate upon it—Kritschewski's thiosulphate phenomenon.[4] Further, it can be expected that quinine may be replaced by mepacrin, or any other new antimalarial agent.

Systematic clinical examinations of the combined treatment suggested above have not yet been undertaken in Japan, but experience has shown us that the most adequate route of administration of thiosulphate is the intravenous injection.

In conclusion we hope that the field of the combined application of thiosulphate as a common, non-toxic activator of chemotherapy need not be restricted to malaria, but will find a widespread extension irrespective of the nature of the chemotherapeutic agent—e.g., sulphanilamide, etc. Out of three cases of kala-azar, resistant to antimony preparations, successful results were obtained promptly through the combined thiosulphate treatment.—We are, etc.,

J. HIRADE.
Y. YASUI.

Tokyo, Japan.

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Poliomyelitis and Lymphocytic Meningitis

SIR,—When presenting his neurological experiences in the Middle East and India at the Royal Society of Medicine, Dr. Douglas McAlpine[1] in his discussion on acute benign lymphocytic meningitis stated that "neutralization tests in some of these proved that the majority were not due to the virus of acute choreomeningitis." He then went on to say that "in 1941 abortive cases of poliomyelitis were reported by Major Caughey, N.Z.A.M.C., thus making the sorting of these cases of lymphocytic meningitis more difficult."

The facts are as follows. Between November, 1940, and July, 1941, an epidemic of poliomyelitis occurred among New Zealand troops in the Middle East. This has been recorded in the *Medical Journal of Australia* by myself and Dr. Porteous.[2] Out of 40 cases 21 were the pre-paralytic type, with changes in the spinal fluid but no paresis. At the time Dr. McAlpine stated in a report that these cases were not cases of poliomyelitis, although they had come from the same division, the same units, and occurred at the same time as the 19 paralytic cases.

In the *Journal* of Dec. 27, 1947 (p. 1019), in a paper on acute poliomyelitis, Dr. McAlpine and others again make reference to acute benign lymphocytic meningitis when discussing the differential diagnosis. When speaking of acute choreomeningitis they state that they "are not convinced that up to the present this condition has been at all common in this country [U.K.], although it should be added that many cases were seen in Service personnel in the Middle East during the late war." There is a marked discrepancy between this latter statement and that Dr. McAlpine made in 1945 at the Royal Society of Medicine. As far as I was aware on no occasion was it established by neutralization tests that acute choreomeningitis occurred in the Middle East among Service personnel, but I am open to correction on this point.

Finally, Dr. McAlpine and others state in the summing-up that in England "the virus of acute poliomyelitis should now be regarded as the usual cause of a benign type of lymphocytic meningitis." Hence they will allow of the diagnosis of pre-paralytic cases of poliomyelitis in the United Kingdom, but Dr. McAlpine persists in his denial of such cases in the epidemic of poliomyelitis in the Middle East. He cannot have it both ways.

I am entirely in agreement that during an epidemic of poliomyelitis by far the most likely cause of cases of acute lymphocytic meningitis is poliomyelitis, but the exact diagnosis can only be made by serological tests and animal tests. Until such are more readily available, during an epidemic of poliomyelitis cases of acute lymphocytic meningitis must be regarded as being due to poliomyelitis.—I am, etc.,

Auckland, New Zealand. J. E. CAUGHEY.

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Fear and Pain in Childbirth

SIR,—Dr. J. Donaldson Craig (April 10, p. 706) makes the point that the pain of labour may be modified, if not entirely eliminated, "by the degree of confidence reposed in medical attendants." A very great deal has been written about the physical pain of labour, but little attention has been paid to what Head describes as "the diminution of general resistance to painful impressions" by "debilitating psychological states, such as anxiety or emotional shock."[1] If certain obstetricians are able to conduct relatively painless labours without anaesthesia, surely it is by the elimination of fear. Is it not time that we devoted more attention to this aspect of the matter?

It is difficult for anyone long familiar with anatomy and accustomed to the facts relating to the physiology of labour to enter imaginatively into the state of chaotic ignorance in which many women are still allowed to approach their first confinement. Ill-equipped with an assortment of half-digested facts about her body acquired from popular medical literature and first-aid classes, the young primigravida waits in the clinic queue next to a loquacious mother of five. She may be encouraged by the resulting confidences, as Dr. H. Thistlethwaite (Feb. 14, p. 318) optimistically suggests, but unfortunately we know that she is more likely to gather a terrifying impression of "instruments" and "stitches." Her own idea of the birth canal must inevitably be that it is small, since her experience of it is limited to coitus and the insertion of vaginal tampons. How can so small an aperture allow the escape of a baby without some ghastly destructive process? As a rule this fear and its associated images are suppressed, and are only shown by an inability to relax during examinations. A simple but graphic explanation about the size of the bony pelvis and the softening processes in the concertina-like vagina will give immediate and lasting relief. If our clinics are too crowded to allow time to probe for these fears, information should be made available to mothers through simple lectures or discussion groups.

The primigravida frequently comes to her confinement in a state of apprehension. In many maternity departments she is admitted in a glare of lights on to a high white bed with a good view of the instrument cupboard. A sterilizer may be boiling up the forceps, presently to be lifted out in front of her, for Mrs. Jones moaning audibly next door. In this year of grace there are still communal labour wards, and she may find herself in the company of one or more pain-weary women more advanced in labour than herself. Confidences are soon exchanged, and they are not such as to reassure. Someone in a white coat appears and examines her. Notes are written and drugs ordered, but remarks to the patient are confined to kindly meaningless phrases which give nothing away and therefore do not allay her fears.

Kindness, though it abounds, is unfortunately not enough. We are all straining to be kind, but custom tends to dull our perception of the inner significance of birth as it is experienced by the mother. It is easy to forget the fear of the unknown and the sense of mystery and miracle which preoccupy her mind while we are debating some obstetric problem. We need to be more sensitively aware of the emotional side of the patient's experience if we are to avoid all those petty unconscious cruelties to which we subject her by our failure of imagination. By eliminating these we may do much to remove the part of pain which is made unendurable by fear, and the fear which may in itself be worse than pain.—I am, etc.,

London, W.11. MARY E. EGERTON.

REFERENCE

British Medical Journal, 1922, **1**, 1.

Pain in Phantom Limbs

SIR,—In discussing the treatment of painful phantom limbs ("Any Questions?" April 24, p. 817) you rightly stress the disappointing results from such measures as excision of neuromata, neurectomy, posterior radicotomy, and stump remodelling operations. You conclude that "the management of these cases is distressingly difficult," but make no suggestion regarding treatment except to advise the patient to persist in the wearing of the prosthesis.

While it is quite true that many heroic surgical measures, including even chordotomy, tend to be ineffective in this condition, it should surely be noted that excellent results are often obtained following 1% procaine injection of the sympathetic nerve supply to the affected limbs,[1 2 3 4] or even from local injection of nerve trunks and scar tissue. The benefit so produced frequently passes off within a short time, but the procedure can be repeated indefinitely and the periods of remission tend to become longer, so that complete cure may result from three or four injections.

It is commonly held that, while phantom sensations are of almost universal occurrence after amputation, actual pain is comparatively rare. In a small series which I have recently studied closely[5] it was found that bouts of pain, sometimes extremely severe, commonly occurred during the first six months after operation. The intensity and frequency of these painful episodes generally diminished with the passage of time, so that by the end of a year or so symptoms were not serious enough to demand treatment other than explanation and reassurance. With only one exception none of these patients has sought advice for symptoms which, although distressing, appeared to them to be so unreal and fantastic as to suggest that they were the product of disordered imagination. One very intelligent subject remarked, "I did not report sick, because I did not expect a doctor to treat a ghost."

It may therefore be that phantom pain is very much more common than is generally believed, and that we are called upon to deal with only that minority of patients in whom spontaneous remission does not occur and who are accordingly driven to seek advice. Amputation inevitably implies nerve injury, and it is therefore reasonable to suppose that in a certain proportion of cases a condition may develop which is directly analogous to the causalgia which sometimes results from other nerve injuries.[6 7] Pain so caused is registered in the sensorium in terms of the established "body image"[8] and so is interpreted as being felt in the phantom.[9]

The persistent symptoms experienced by such patients are very real indeed, despite the frequent paucity of demonstrable abnormality in the stump, and they may lead to complete breakdown of physical health and emotional stability, as in one unfortunate case in my experience. Therefore, although the difficulties and disappointments in treatment are realized, it is suggested that a largely nihilistic therapeutic approach is unjustified when simple methods of proven efficacy are available.—I am, etc.,

J. DONALDSON CRAIG.

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Treatment of Pruritus Ani

SIR,—The variety of methods of treatment and the frequent therapeutic failures in pruritus ani are probably due to a lack of recognition of the fundamental cause of the complaint. This cause, however, is always the same. It is the exposure of the perianal skin to particles of faecal matter. The perianal skin normally possesses a specific resistance against the irritation set up by adhering particles of faeces following defaecation. Occasionally, however, this resistance breaks down. This usually happens in middle and old age, more seldom in younger individuals, and practically never in the young and adolescent. Once an irritation has set up, there develops a vicious circle. The irritation gives rise to scratching and excoriation, the faecal particles penetrate into the crevices of the damaged skin and aggravate the irritation, and so it goes on until a kind of perianal eczema develops.

The rational treatment therefore has to be both palliative and causative. The most suitable palliative treatment proved to be radiotherapy. Three doses of 100 to 150 r at weekly intervals of a radiation produced at 90 to 100 kV and filtered through 1 mm. of aluminium are usually sufficient to clear up the eczematous condition. In some cases a fourth treatment after one more week may be required.

The treatment is best given with the patient in the knee–elbow position and the buttocks pulled apart so as to expose the anal region. The width of the field depends on the extent of the skin involved. When large fields are used it is necessary in male patients to protect the testicles by a sheet of lead or lead-rubber.

The causative treatment, which should be begun at once, consists in washing with soap and water the anal region after every defaecation. Not only must the surrounding skin be washed, but the lining of the anus must also be cleaned by pushing the soaped finger inside it. All traces of soap must be rinsed away with water, the skin dried, and a dab of calamine lotion applied to the area. This treatment must be rigorously carried out indefinitely if recurrences are to be prevented.

This treatment has been uniformly successful in over 50 cases of pruritus ani. The few recurrences observed occurred only where the patient omitted to carry out the washing, and a final cure was achieved when regular washing was resumed. Mild cases may yield to washing alone without *x*-ray treatment. Occasional irritation may be relieved by one or two applications of "nestosyl" ointment.—I am, etc.,

St. Peter Port, Guernsey. ALEXANDER ORLEY.

D.D.T.

SIR,—In the leading article entitled "D.D.T. in Use" (April 3, p. 648) you list the drawbacks of this insecticide and discuss briefly the ways in which these may be overcome. One or two points were made, however, which, we venture to suggest, require further consideration.

It was stated that D.D.T. is apparently lethal to all insects and acarines. That is, in our opinion, a somewhat arbitrary statement, as D.D.T. is certainly not lethal to all acarines—the glasshouse red spider being a case in point—nor is it toxic to all insects. Much work will have to be done before anything like complete information is available as to the relative toxicity of D.D.T. to arthropods in general, but with our present knowledge and methods of formulation your statement is incorrect.

The several problems of irritancy, the lag in aquiring a lethal dose, and the non-persistence of D.D.T. have to a considerable extent been overcome with those insects susceptible to it by scientific formulation and new and improved methods of application. One of us (F.G.S.W.), while carrying out trials at the Royal Naval School of Tropical Hygiene, Colombo, and later in this country, obtained excellent results against flies, mosquitoes, cockroaches, and bedbugs using the new activated emulsions evolved by Dr. H. Hurst, with greatly improved knock-down and residual toxicity. Using these emulsions there is little possibility of mosquitoes escaping from rooms with non-lethal doses, and the residual toxicity against cockroaches (among the most resistant of insects) has been proved to be effective for six months or more in such unfavourable surroundings as canteens and kitchens. Comparably good results have been obtained against flies on cattle.

The work of Twort[1] on heat volatilization of germicides has established the method of the production of insecticidal aerosols by a similar means. A continuous aerosol of D.D.T. produced by controlled heat at the rate of 20 mg. per hour per 3–5,000 cu. ft. (85–141 cu. m.) will give a complete knock-down of many diptera within 30 minutes or less. Furthermore, by this method the use of solvents is obviated and any loss of efficiency due to supersaturation is eliminated. What is of extreme importance is that a film of crystalline D.D.T. is continuously being deposited on all surrounding surfaces, and those which are highly porous will tend to have losses by absorption balanced by the continuous deposit of the aerosol. Even fabrics hung in a room in which a continuous-phase aerosol is being produced will, in time, become toxic to clothes moths.

With regard to cattle, field trials carried out last summer showed that the application of continuous-phase aerosols in the sheds for periods of as little as three hours daily gave immunity from biting flies both in the byre and at pasture.

The irritant effect of D.D.T. when not specifically formulated for quick knock-down may not in all cases be as harmful as may at first be apparent. Col. J. W. Scharfe, R.A.M.C.,

when serving as the military member of the Medical Advisory Division, S.E.A.C., was of the opinion that relatively light contact by mosquitoes with walls sprayed with a 5% solution of D.D.T. in kerosene resulted in a "biting inhibition" reaction which prevented the insect from feeding, either by an initial peripheral paralysis or by loss of appetite caused by the D.D.T. This effect has been noted recently with the stinging of wasps in Sweden and with *Stomoxys* in this country.

Concerning the lack of toxic vapour we have clear evidence that vapours emanating from screened surfaces painted with D.D.T. are lethal to flies in enclosed spaces, though whether directly or by readsorption on to treated surrounds has not been determined.—We are, etc.,

F. G. SAREL WHITFIELD.
A. H. BAKER.
L. J. WHITE.

Avebury Laboratories, Goring-on-Thames, Oxon.

REFERENCE

1 *J. Hyg., Camb.*, 1940, **40**, 321.

Curare in Treatment of Spastic Conditions

SIR,—Drs. C. Astley Clarke and R. D. Hotston (Feb. 14. p. 289) report that curare in oil and wax had no advantages over the aqueous preparation in duration of effect or avoidance of side effects. With an air of finality they concluded that curare in oil is not the hoped-for advance in reducing spasticity.

With their findings one can have no quarrel The implication that they have set up a critical comparable experiment with previous work is, however, fallacious. Their entire experiment was carried out with a suspension of *d*-tubocurarine in oil and wax supplied by Burroughs Wellcome and Co., whereas previous material was made up by the experimenter himself and later by E. R. Squibb and Sons. Suspensions in themselves vary with the techniques of the makers, and potency assays from manufacturer to manufacturer have varied greatly. This is common knowledge. There remains then a great weakness in the nature of your authors' conclusion from their experiments. A more acceptable and less sweeping conclusion would be that Burroughs Wellcome curare in oil and wax did not yield any more favourable results than aqueous curare.

I might add that spasticity is frequently a moiety of syndromes exhibiting weakness, ataxia, involuntary movement, and contracture. A critical evaluation, therefore, of its amelioration by any agent obviously requires careful study. Such study should include recording of range of motion changes, variations in stretch response as judged clinically and by myography, motion pictures of motor function, and whatever other data can be gleaned from the skills of the physiotherapist and neurologist. Static deformities must be exempted from the experimental group treated. Such data cannot be extracted from clinical observations of, "Did the injections enable a bedridden patient to walk or allow an ambulatory one to discard a stick ?"—I am, etc.,

New York. EDWARD B. SCHLESINGER.

Pancreatitis Due To Ascariasis

SIR,—I feel that this case is of sufficient interest to warrant a short description.

A boy of 18 months was admitted to hospital with a history of diarrhoea with blood and mucus, and a rectal prolapse, for three weeks. Examination showed a very thin baby with tense distended abdomen, liver slightly enlarged, a small readily reduced rectal prolapse, and temperature of 100° F. (37.8° C.). No other abnormality was found. The stools were very pale and bulky, offensive, and contained much free fat. They were unaffected by diet, and microscopy disclosed ascaris ova. The third day after admission a mass became palpable under the costal margin, just to the left of the midline, and santonin treatment produced two adult ascarides. Over the next eight days the mass slowly and steadily enlarged, with steady deterioration of the child's condition. The temperature swung irregularly between 101° and 97.6° F. (38.3° and 36.4° C.).

On the ninth day after admission consent was at last obtained from the parents, and the mass was explored under local anaesthetic. An abscess cavity adherent to the abdominal wall was opened and 6½ oz. (190 ml.) of greenish-yellow pus with a sweetish smell was evacuated. The patient's condition precluding further exploration, a small drain was inserted and the skin protected with sterile vaseline. The following day there was a profuse yellowish serous discharge and the drain was removed. The fourth day after operation slight digestion of the wound edges was noted, and the following day, the fifth after operation and the fourteenth after admission, the patient died.

Post-mortem examination disclosed an abscess cavity occupying the whole of the head of the pancreas, extending some 3/4 in. (1.87 cm.) to the left of the midline, and containing the partially digested remains of an adult ascaris. A track extended upwards retroperitoneally, entered the liver, the whole of the left and quadrate lobes of which were destroyed, and discharged through an incision at the left costal margin. In the small intestine a further seven ascarides were discovered.

In the rather limited literature at my disposal the only references I can find to a similar occurrence are those of ascaris being a rare cause of acute pancreatitis in Craig and Faust, *Clinical Parasitology* (4th edition, 1945, p. 342), and Rose and Carless, *Manual of Surgery* (7th edition, p. 1314).

My thanks are due to the Acting Director of Medical Services, Tanganyika Territory, for permission to publish this account.

—I am, etc.,

Chunya, Tanganyika Territory. N. A. DUNCAN.

Stasis of Chest Radiographs

SIR,—When a tuberculous patient moves from one district to another it is the practice of most tuberculosis officers to send the chest *x*-ray film to the colleague who is to take over the case, and these are often useful for comparison with subsequent films. The more enlightened voluntary hospitals also co-operate in this respect when they transfer patients to tuberculosis clinics. Sometimes, however, it is extremely difficult to obtain such films, not only from hospitals but even from Government departments.

It may be that this reluctance to part with *x*-ray films is due to the fear that they may be lost, but for practical purposes they may be just as much lost in the archives of some distant institution as if they were at the bottom of the Atlantic. True, some of these film-hoarders send clinical and radiological reports, but it is impossible to compare a film with a report. Surely when a patient moves from one clinic to another his chest *x*-ray film, often the one concrete piece of evidence in his medical history, should follow him like his more orthodox shadow.

The day draws near when the tuberculosis officer is to be enmeshed in the net of Governmental and voluntary hospital control, and he too may become a film-hoarder. Before the net is finally drawn, however, perhaps one last pleading wriggle may be permitted in this matter of the free circulation of chest *x*-ray films.—I am, etc.,

Worcester. R. B. MAYFIELD.

Treatment of Undulant Fever

SIR,—The present unsatisfactory state of treatment of undulant fever is stressed in the annotation under this title in the *British Medical Journal* of Nov. 1, 1947 (p. 700), which prompts me to record my experience in the use of "suramin," ("germanin," "Bayer 205," or "antrypol").

Since it is rare for any one physician to have a sufficient number of cases under his care for a controlled experiment, and since the course of the disease is so unpredictable as to make conclusions drawn from a small number of cases hazardous, it is hoped that others will take steps to use this simple method of treatment and record their results, so as to confirm or refute its apparent efficacy.

So far as I am aware, suramin was first given for this purpose in 1930 by Dr. J. Leggate, of Salisbury, Southern Rhodesia, in consultation with me. The patient, an adult male European, had been ill for four months, and a blood culture revealed *Brucella abortus*, which his serum agglutinated to a titre of 1/50. The dosage was 1 g. suramin in 10 ml. of sterile distilled water intravenously once a week for four doses. The first dose caused some exacerbation of pyrexia and of symptoms, but after the second injection there was a gradual improvement, and convalescence began after the third dose.

Since that date the drug has been used by me for seven cases whose diagnosis had been definitely confirmed by positive blood culture. Satisfactory results were obtained in all of them.

The details of the procedure have varied somewhat, but the method now adopted is as follows :

As soon as a pyrexial period commences, 1 g. of suramin in 10 ml. of sterile distilled water is injected intravenously. This is usually followed by an exacerbation of symptoms and of pyrexia over the subsequent one to two days. A week later a similar injection is given. No exacerbation has been noted, and there is a tendency for the pyrexial curve to pass into a rapid lysis over the next two or three days.

In five of the patients a further pyrexial bout started and in these a further injection of 2 g. was given, with disappearance of all symptoms within 48 hours. In the other two cases two injections sufficed.

No treatment other than symptomatic was given, but in view of the well-known effect of suramin on the renal tubules the urine was examined daily for albumin and casts. On the above dosage neither was demonstrated on any occasion. The following is an illustrative case.

A European male aged 20 was admitted to hospital on Feb. 18, 1941, with a history of 6 days' headache, backache, shivering, and joint pains of insidious onset, the latter not relieved by adequate doses of aspirin ; two days' drenching sweats, especially at night; sudden onset of acute pain, lasting for one day, in right knee, right big-toe joints, left ankle, and left elbow, all of which were red, swollen, and distended with fluid.

On admission, T. 102.2° F. (39° C.), P. 128, R. 26; in extreme pain; appearance as of an acute gonococcal case with complications but no urethral discharge and no gonococci in prostatic smear. There was a mild secondary anaemia, with W.B.C. 12,500 (polymorphs 68%, lymphocytes 30%, eosinophils 2%). Blood culture in broth and in blood-broth sterile. No agglutination to typhoid or *Brucella* groups on Feb. 19 and Feb. 24, 1941.

The treatment given was 1 g. sulphapyridine 4-hourly for 6 days, with an intramuscular injection of 1 g. soluble sulphapyridine twice daily on Feb. 19 and 20. This had no effect on the pyrexia, the acute joint pains, or the orchitis. By March 1 the temperature had returned to normal but the chart was " undulant " in character.

On March 4 a new pyrexial phase started and further blood cultures in blood-broth were taken. One specimen was incubated under normal conditions and one under 10% CO_2 tension; only the latter grew " an organism having the biochemical and agglutination reaction of *Br. melitensis*." On March 5 the first injection (1 g. suramin) was given intravenously. A mild exacerbation of pyrexia was noted but no increase in joint or testicular pain. On March 12 the second injection was given. There was no immediate effect, but from March 15 the temperature slowly subsided, to become normal on the 20th.

On March 23 the third pyrexial phase started and 2 g. of suramin was given on the 24th. During that night the testicular pain disappeared, but the joints were still very painful; temperature (8 p.m.) 102° F. (38.9° C.). The following day the temperature did not exceed 100° F. (37.8° C.) and was normal on the 26th. He was discharged from hospital on April 23 and was seen at intervals for nine months. No relapse occurred.

This case illustrates the following points : (*a*) the uncommon type with acute joint involvement; (*b*) the rare epididymo-orchitis (cf. Straus's reaction); (*c*) the failure of sulphapyridine; (*d*) the need for CO_2 tension for success in blood culture; (*e*) the method of treatment advocated.

Suramin is one of the symmetrical urea derivatives, and there is some laboratory evidence that it has an inhibitory action on the *Brucella* group.

A personal communication from Dr. M. Gelfand, of Salisbury, reports a further successful treatment by this method in a patient seen by him in consultation with Dr. Nuttall Smith, of Gatooma, who carried out the treatment.—I am, etc.,

S. Rhodesia Government Medical Service. R. M. MORRIS.

Idiosyncrasy to *d*-Tubocurarine Chloride

SIR,—May I comment on the article by Drs. T. Cecil Gray and John Halton (April 24, p. 784) on this subject? I was surprised to read that 15 mg. of *d*-tubocurarine chloride had been used on their first case as an initial dose. Surely there are very few anaesthetists who have not realized that such a dose is excessive. Previously I have advocated an initial test dose of 5–10 mg., followed by minimal additions, owing to individual susceptibility (*British Medical Journal*, 1947, **1**, 267). My further experiences have more than justified this belief.

The use of a pharyngeal airway when inflating the lungs must be condemned for two reasons—namely, (1) distension of the stomach, and (2) regurgitation of fluid from the oesophagus to the air passages. To obtain a clear airway, intubation in the majority of cases is quite unnecessary with the glottis paralysed by *d*-tubocurarine chloride. However, it becomes essential when inflation is carried out, in order that a pack can be inserted in the pharynx or a cuff-tube in the trachea, either of which will avoid the above complications.

Blood-stained fluid was regurgitated and entered the air passages during the 195th minute, from which time the patient's condition appeared to deteriorate rapidly. The routine use of a cuff-tube or a pack before inflating the lungs would have avoided this catastrophe. However, it appears that in spite of this mishap Case 2 was again subjected to the danger of regurgitation into the air passages, not to mention the effect on the stomach of intermittent distension for 45 minutes.

I am in full agreement with Drs. Gray and Halton in re-emphasizing the importance of a trial dose, although I consider 1 mg. per stone sufficient as the initial dose for a child.—I am, etc.,

Swansea. D. S. JONES.

Malignant Syphilis

SIR,—Dr. C. D. Alergant (April 17, p. 757) appears to be critical of the medical memorandum written by Dr. W. Fowler and myself, entitled " Malignant Syphilis " (March 6, p. 457), and we would like to make the following comments :

1. The diagnosis was not at any time in doubt. In addition to the evidence in favour of syphilis which we published, the patient was also seen by Dr. J. T. Ingram, consulting dermatologist to the Leeds General Infirmary, who was also satisfied that the patient had syphilis. It is our experience, and that of most authorities we have consulted, that it is extremely difficult to find *S. pallida* in rupia or other very late secondary syphilitic eruptions.

2. We are accustomed to using very large doses of penicillin, arsenicals, and other drugs in the treatment of syphilis, but did not do so in this case because we were convinced that the slightest therapeutic shock would have precipitated his death. It was not merely a question of combating virulent infection but of endeavouring to keep alive a patient who from the time we made our first examination was almost moribund from severe and long-continued toxaemia.

3. It has been our experience that it is very difficult to infect rabbits with material from human syphilis. To have made this experiment when the patient was first seen would have meant subjecting him to unnecessary manipulations, thereby increasing his weakness.

4. The question of therapeutically inactive penicillin can be excluded because many other patients suffering from syphilis were treated with the same batch of drug, which was in general use in the hospital, and no suspicion of lack of potency was aroused.

—I am, etc.,

Leeds. ROBERT LEES.

The Fenestration Operation

SIR,—With reference to the recent communications in your *Journal* on the above subject I should like to suggest that the newly formed Otolaryngological Group Committee of the B.M.A. should appoint a special research subcommittee from the most suitable members of the Group to collect the data submitted to them on request from all surgeons who have performed these operations. A national record should be kept of their results and the findings of this subcommittee should be issued through the *British Medical Journal* at regular intervals up to a period of ten years, so that the medical profession and, through them, the public will be able to reach a true assessment of the value of this operation in this country, being guided by such a body of experts. A questionary could be drawn up and sent out to cover all data required, both pre- and post-operative. Already much data is available compiled on a scientific basis.

I understand that Dr. Julius Lempert, of New York, who is shortly to pay us a welcome visit to this country, claims to have operated on several thousand cases, but we want to know the British findings. It was in this country that early pioneer work was done by Jenkins, Fraser, and the late Dr. A. A. Gray, before Mr. Lempert improved the technique and so made the operation practicable. The report would stimulate further research concerning otosclerosis, the cause of which is so little understood at present.

Medical opinion is much divided in this country, even among our most eminent specialists, as to the final results of this operation. Time is an essential factor. The success of this operation and its recognition by the medical profession depends

upon the most perfect operative technique and the most careful selection of only the most suitable cases of otosclerosis. Nothing will bring the operation into greater disrepute than bad results by operating in unsuitable cases.—I am, etc.,

Ewell, Surrey. GORDON C. HENRY.

The Nelson Touch

SIR,—"Serving Officer" (April 17, p. 750) need not worry over the revelation of names of V.D. cases to his commanding officer. He has not been in the R.A.F. long enough to forget he was once a doctor. Let him neglect to carry out this disgusting order. A colleague and I refused to comply with it when promulgated in this command six months ago. No direct action has been taken against us. Of course we should have been court-martialled and dismissed or even cashiered long ago. Our confidential reports must be close to the "adverse" level, though. That such a violation of confidence is performed uncomplainingly by the majority of medical officers is a sign of the times.—I am, etc., FLIGHT LIEUTENANT.

Colonial Medical Service

SIR,—From the Annual Report of Council (*Supplement*, April 10) at p. 94, it might be deduced that all that is wrong with the Colonial Medical Service is inadequate salaries. It appears also to be the Colonial Office view that since Colonial Governments cannot or will not pay more there is nothing to be done but hope that in time austerity and unemployment at home will force men into the service. But surely all medical men do not ask first where and how they can find most money?

In the colony that I have left private practice was probably better than in most others, and on average brought total incomes to a reasonable level. Yet the situation was (mid-1947): (i) The shortage of medical staff was between 30 and 40 on an authorized establishment of 99 all branches. (ii) The wastage from invalidings and resignations was unparalleled in any other department. (iii) Only about one in four entrants completed service to age 50. (iv) Many stations which used to have M.O.s were being worked by dispensers or nurses only; others no longer had M.O.H.s; the larger hospitals were badly understaffed. (v) Shortage compelled the retention in the service of passengers who brought discredit on it. (vi) Of the Government's promises to the people during the planning years of extended medical services, requiring a large increase in staff, nothing had come. (vii) Morale in the department was very low. All this, in spite of the facts that there is so much in the work of extraordinary interest, and so much in the life attractive to tough, enterprising, and restless persons; and that colonial was accepted as an alternative to military service.

I would suggest that the most important cause of the unpopularity of the service and the general dissatisfaction within it is the colonial civil service atmosphere in which we have to live and work, and the sort of administration and type of administrator we have to endure. Quite how soul-searing this is is difficult to describe briefly. To a remarkable degree the old tradition persists from the days when every man in West Africa had a "history" of treating staff rather as potential breakers of regulations and blotters of copy-books than as professional men doing work of some value.

For many years now the higher administrative appointments have with rare exceptions been filled from the numerically much smaller Health Branch—that is, by men who have spent almost the whole of their service in the relative ease and comfort of health offices, with little if any experience of the remote and lonely bush stations or of heavy work in the larger hospitals. Most of them soon develop a type of mind which makes inevitable disharmony between themselves and the working staff. Not long ago our head office staff were known collectively as the Old Men of Vichy. One director inspecting my hospital carefully examined the insides of all the drawers and cupboards, outside taps to see if they were leaking, and some disused latrines. That was all; of the work of the hospital, not a word. Another in the course of a little dispute barked out, "This is not a democratic service, it is a semi-military one."

There is no freedom of expression of opinion, and the medical staff have no means of influencing either the Colonial Government or the Colonial Office. If the trouble is taken to draw up and present a memorial, it will merely get the usual dusty answer. If an individual criticizes or expresses opinions unwelcome in head office, he may be regarded as having permanently blotted his copy-book and forfeited all claim to consideration and promotion—and very likely be sent to a punishment station (I have been myself). A colleague who sent a brief signed letter to a journal drawing attention to a misstatement in the advertisement was officially informed that he had thereby incurred the displeasure of the Secretary of State. Such offences are more serious than almost any degree of idleness or dissolute living.

In war it is realized that morale is all-important not only in the fighting services but among civilian workers. It is surprising and lamentable that it should have been so neglected in the Colonial Service. I see little hope of progress until there is installed as director-general at the Colonial Office one with a powerful personality who will be a great deal more than a mere Civil Servant and who will command the respect and the liking of the staff. At present there is only a small advisory staff consisting of retired administrators none of whom have ever meant anything to us in the Colonies.

Those who think there is nothing to fear in a whole-time salaried State service would do well to look closely at the Colonial Service. Not so long ago Dr. H. B. Morgan, M.P., then in opposition, alleged in the House that it was a disgrace. Very recently, supporting Mr. Bevan, he claimed that it was quite satisfactory. I think most of us would say he was nearer the mark first time.

As a retired (specialist) colleague remarked, it might have been a grand service, but the direction is all wrong. I have enjoyed it, and do not regret my choice, but would not now recommend it to one in search of a career unless he was very sure that his tolerance of "the direction" is and will remain without limit. Mine was not.—I am, etc.,

G. L. ALEXANDER,
Bristol. Colonial Medical Service (ret.).

POINTS FROM LETTERS

Resident Appointments

UNEMPLOYED DOCTOR writes: During the present fantastic scramble for resident hospital appointments considerable time and anxiety could be spared the applicants if the following simple procedures were adopted by the hospitals concerned: (1) Appointments are only advertised if there is a definite vacancy not likely to be filled by a candidate already known to the appointing committee, or that the existence of such a candidate be indicated in the advertisement. (2) Appointing committees only short-list a candidate if they consider him fully suitable for the appointment, and not merely to make their meeting official. (3) Immediately the short list is compiled, candidates whose names do not appear on it are notified to that effect.

John Hilton

Drs. ELLIOT E. PHILIPP and E. W. WALLS (Middlesex Hospital Medical School, London, W.1) write: We are preparing an entirely new edition of John Hilton's surgical classic *Rest and Pain*, to be published by Messrs. G. Bell and Sons, Ltd., the publishers of the original lectures. We should be most grateful to any of your readers who can give us any information that might help us in this work. As we propose including a short biographical note on John Hilton we would welcome details of his life—especially his early life—and the temporary loan of any portrait that may be suitable for reproduction.

O.H.M.S.

Dr. H. G. HOWITT (London, S.W.16) writes: I have already received complaints about the new method of dealing with national health certificates by the Ministry of National Insurance. One patient complained that correspondence with the Ministry over sickness certificates had cost a shilling in postage. In the past an insurance agent had called and paid cash. I advised her to let the Ministry pay postage in future.

Fainting at Immunization Sessions

Dr. N. J. W. THOMPSON (St. Helens) writes: When carrying out diphtheria immunization on large numbers of school children I find that a certain number, say 2%, succumb to fainting attacks. . . . The attacks come on during, after, or sometimes even before inoculation. Nervous apprehension seems to be the provocative factor, and delicate or highly strung children seem the most susceptible. In dealing with such cases I find the following procedure very useful. I instruct the child to squat down, sitting on his heels. I then tell him to clasp his legs and press his thighs tightly against the abdomen. This manœuvre, by squeezing the blood from the splanchnic area, raises the systolic and diastolic blood pressures by 15 to 30 mm. Hg. Cerebral circulation is quickly restored and the child recovers in a few minutes.

Festina Lente

Dr. W. REGINALD WILSON (Doncaster) wires: Imperative retain ownership and settle about consultants and chemists and certification before assenting. Festina lente.

Obituary

ERIC GUTTMANN, M.D., M.R.C.P.

Eric Guttmann was born in Gleiwitz, Upper Silesia, and spent the first half of his professional career in Germany. He came to this country in 1933. He died on April 25 at the age of 52.

Guttmann's training, on his own initiative, was more than usually broad and thorough. After qualifying, he studied pharmacology before specializing in neurology in the clinically oriented school of neurology in Berlin under the leadership of Cassirer, Oppenheim's successor. He then went to Munich and studied psychiatry under Kraepelin and neuropathology under Spielmeyer. He became Lange's chief assistant at the Psychiatric Research Institute in Munich, and acting director there until he followed Lange to Breslau. With the beginning of the Jewish persecution he came to England in 1933 with the help of the Rockefeller Foundation. At the Maudsley Hospital he was one of the principal workers in the Department of Clinical Research until, at the outbreak of the war, like all others in his position, he was interned for a time. Subsequently he worked in the neurosurgical department at the Radcliffe Infirmary at Oxford and in the Neurosis Centre at Mill Hill Emergency Hospital. When the Maudsley Hospital was reopened he returned there and was assigned the arduous and anxious task of supervising the complete reorganization of clinical teaching there.

His chief work was in research and his main interests were in neuropsychiatry, in the investigation of the psychological phenomena of organic disease. His interests were wide. He was responsible for introducing the use of amphetamine in psychiatry, and his papers on the mescaline psychosis and on the artistic productions of psychotic patients awakened general interest. His work on the psychiatric aspects of head injuries is a permanent contribution to our knowledge. He did much other valuable work, on the functions of the frontal lobes, on meningiomata of the brain, on Schilder's disease, Huntington's chorea, the psychological aspects of general bodily illness, and on prognosis in schizophrenia. Social psychiatry, which came into prominence during the war, also engaged his attention. He was the psychiatric consultant to the Officers Selection Board of the National Fire Service, and later he carried out for the Ministry of Health an inquiry into the after-history of neurotic soldiers, the results of which have recently been published. His research work was characterized by catholicity of interest, breadth of learning, balance and coolness of judgment, and by thoroughness and caution.

Inevitably, as he was attached to a teaching hospital, he spent much time in teaching. From the time of his arrival at the Maudsley he exercised a considerable influence on his younger colleagues. Through him the Meyerian approach, which had been the dominant influence at that school, was broadened by phenomenological conceptions such as the possibility of analysing symptoms into those directly due to a basic organic process and those which represented a reaction of the personality. His clinical acumen and diagnostic powers were such as to give convincing evidence of the validity of the principles he taught. His teaching was seen at its best at the bedside, or in the discussion of fundamentals over coffee or tea. But he was an able lecturer, and he became part author of a well-known short textbook of psychiatry for medical students. Privately, and disdaining any acknowledgment, he gave generously of his time in helping his junior colleagues with their own work, whether it was research, the clinical problems of the wards, or aid from his knowledge of theory and extensive acquaintance with the literature. In his last years, when his main preoccupation was the training of postgraduate students, he won their affection and respect by his accessibility, his lucidity in exposition, and his clinical wisdom.

As the laws of chance require, there are men doomed to go through life with a more than average share of misfortune. Guttmann had qualities to put him in the first rank, yet he never attained an independent position. His career was twice completely disrupted, first by having to leave his native land, and again at the outbreak of war. Finally, when he seemed on the point of reaching the position his merits deserved, his health failed. Yet he was a man of genial and happy disposition. He gave all his loyalty to the land of his exile. With his deep kindliness and self-effacing reserve he found himself at home in the temperamental pattern of English life. It was impossible not to be friendly with him. He met his misfortunes with the dry ironic humour and the courage and good will that marked his personality and endeared him to all who knew him. He is survived by the son and daughter of his first marriage, and by his wife, Dr. Elizabeth Rosenberg, and an infant son.

A. L. writes: No one could replace Eric Guttmann in the affection of his friends, and it is very doubtful whether anyone can replace him in the remarkable contribution he was making to psychiatric research and the training of psychiatrists. From the time of his arrival at the Maudsley in 1934 it was clear that a man of outstanding capacity had come who was prepared to devote all his gifts, without thought of personal advantage, to the furtherance of sound psychiatry in this country. His integrity and friendliness, and the respect his abilities always evoked, soon made him a trusted adviser in all the clinical activities and the development of the medical school; every one of his colleagues learnt much from his unusual combination of sound, experienced judgment and fruitful scientific and therapeutic enterprise. He was versatile but never superficial; critical yet encouraging; and always to be relied on for unselfish, unlimited help. His tact and sure perceptions made him almost ideally successful in his dealings, whether with his colleagues, his pupils, or his patients and their relatives. When the Maudsley resumed its normal work after the war Guttmann showed a characteristic disregard for his own interests and convenience. He knew, though his friends had no inkling of it, that he had a cardiac lesion which had given threatening signs, but he willingly shouldered a heavy burden of teaching and clinical duties; he enjoyed the work intensely, and many young psychiatrists have abiding reason to be grateful for the guidance and stimulus he gave them during those two post-war years at the Maudsley. So also have his senior colleagues. By his writings and research, and still more by his direct teaching and example, Guttmann exercised upon the growth of psychiatry in this country a steady and increasing influence the full extent of which can hardly yet be appreciated. He gave this unsettled branch of medicine a sure impetus, brought it closer to neurology, and by his command of psychological and other research techniques, allied to wide clinical experience, showed the way of sound progress. But it is his generous spirit, his kindness, his humour and courage that his friends now remember with a feeling of intense personal loss.

Dr. CHARLES SHACKLETON SIMPSON, who was born at Brighton in 1861, died on April 21 at his home in Hove. He had retired from active practice some seventeen years ago. He had been bed-ridden for two years, and looked to his end with equanimity, for he was unable to enjoy the fruits of his retirement, his garden, his books, and his music. He came of a talented family of architects, his father having designed much fine property in Brighton. Two other brothers were similarly engaged—one, Sir John Simpson, was P.R.I.B.A., and designed Wembley Exhibition and Roedean School. A third brother was professor of surgery at Sheffield. Educated at Brighton Grammar School, Charles Simpson studied medicine at Guy's Hospital and qualified in 1889. After holding some junior appointments he settled in Hove, where he practised for forty years. He did much hard and useful work and was greatly loved and respected by all. He gave unfailing courtesy, kindness, and consideration, and had a quiet bedside manner together with a keen sense of humour. He refused to argue or get ruffled, thus preserving a peace of mind which he loved in his household and fireside. Rush and hurry were foreign to him, though he always had time for everything. For many years Dr. Simpson took a great practical interest in a local Scout troop. He was a keen naturalist and ornithologist and was interested in photography. He was a great reader, and also had a magnificent library of gramophone records. Throughout his career there were no outstanding honours or publicity, no display, just plenty of hard work. He had many an interesting and amusing tale to tell of past decades when walking, horseback riding, cycling, and carriages preceded cars. He also told of typhoid, which was very common in the old days, and of the period when teeth were extracted with an

instrument like a key, the operator keeping his top hat on during the process and the tooth jumping up to the ceiling.

When he retired many mourned his going and inquired about him long afterwards. Charles Simpson had a broad tolerance and understanding of new ideas and youth, together with a practical knowledge of clinical medicine. He had the true Christian spirit. Sympathy is offered to his wife, who looked after him so well in health and sickness, and to his two daughters.—J. H.

Dr. WILLIAM FRANCIS CHRISTIE, who died at Stibbington on April 25, was the son of the late Dr. Dugald Christie, C.M.G. He came from a large family, of whom a number entered the medical profession, including Prof. R. V. Christie, of St. Bartholomew's Hospital, and Dr. J. M. Christie, of Finchley. Coming from Edinburgh with an outstanding athletic record, and after a not undistinguished academic career, Christie first entered the R.A.M.C. as a regular officer. He served with distinction during the 1914–18 war and in India. He had graduated M.B., Ch.B. in 1909, and he proceeded M.D. in 1919. On retirement in 1923 he went into practice in Lancaster Gate, London, where he remained until recalled to serve as a medical specialist during the 1939–45 war. At the end of the war he did not return to practice but retired to a beautiful old rectory near Peterborough. At one phase of his career Christie became interested in obesity and was the author of two popular books on this subject. These were a happy combination of scientific fact and cynical humour, presented in a language which could be understood by the laity and illustrated by a famous artist with drawings which emphasized how much the lusts of the flesh contributed to a pathological state. "Willie" Christie was a first-class tennis player and was a regular tournament competitor until the last war. He had a large circle of friends, both inside and outside the profession. He was a natural host, a charming companion, and a good friend to many. In his practice he combined kindness and tact with shrewdness and ability. These characteristics were invaluable to him in dealing with his many important patients, to whom he often had to give unwelcome advice. He is survived by his widow, Cecil, daughter of the late Sir Abe Bailey, whom he met when she was nursing during the 1914–18 war. There were no children.—L. W.

Medico-Legal

LIBEL ACTION BY MR. MATTHIAS ALEXANDER

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The evidence given during the first nine days of the hearing of this action for libel was reported in our issue of March 20 (p. 575). The plaintiff was Mr. Frederick Matthias Alexander, of London, and the defendants were three medical men, Dr. Ernst Jokl, Physical Education Research Officer to the Union Education Department, Dr. E. H. Cluver, Director of the South African Institute for Medical Research at Johannesburg, and Dr. B. Maule Clark, of Houghton, Johannesburg, as editors of *Manpower*, a biannual scientific journal published in Pretoria by the Government Printer and circulating throughout the Union.

Mr. O. Pirow, K.C., addressed the court for the defence.[1] It relied, he said, on the plea of prescription, that the action had been brought after the statutory period of one year had expired; and on the pleas of justification and fair comment. The evidence showed that Mr. Alexander was an ignorant layman who knew very little of anatomy and physiology yet claimed that healing or therapeutics was "his own province." His five books were useless as textbooks for his technique or as guides to health or to a philosophy of life. They could be read only as "sales talk." They tried to eliminate all possible sources of competition as incomparable or harmful. As against the "incompetence" of the medical world, the "humbug" of faith healing, and the "quackery" of physical education, Mr. Alexander claimed that his technique was unique, that it had a practical procedure that would prove the keynote of future evolution, and that its practice would eradicate and prevent all disease. This he supported with the equally revolutionary contention that all disease really originated in erroneous preconceived ideas of the use of the body and the self. Mr. Pirow submitted that these claims had been completely disposed of by the medical evidence. If his claims to provide an unfailing preventive to disease were held to constitute quackery, that disposed of the case.

The fact that Mr. Alexander might improve posture by manipulation and provide other qualified benefits was beside the point. His claims covered the whole field of pathology from cancer to hay-fever. The evidence about the technique boiled down to achieving a certain posture and receiving certain manipulations; from these and a certain head–neck relationship certain remarkable benefits were claimed, but there was no evidence properly establishing a relation between the action and the alleged benefit. Sir Henry Dale had given evidence that the support of such eminent laymen as Sir Stafford Cripps and the late Lord Lytton could be looked upon as "a typical instance of group hystero-neurosis." Most of Mr. Alexander's cures seemed to have affected people afflicted with some form of anxiety neurosis.

Case for the Plaintiff

Mr. H. J. Hansen, K.C., submitted for the plaintiff that the article complained of was a complete misrepresentation of the principles of Mr. Alexander's teaching.[2] It omitted all references to the method of teaching—the inhibition of the old wrong manner of use and the substitution of a new right use in which the head–neck relationship was of prime importance. Nor was there any reference to the theme that the results of this right posture and body mechanics would correct old strains and misuses and would strengthen man's resistance and thus in time make him immune to disease. Dr. Jokl was not concerned with Mr. Alexander's claims in their medical or educational aspect, but only as they affected physical education, of which he was a protagonist. The setting in which the article was written was the suggestion that Mr. Alexander was making false claims about the benefits of his system on health as compared with physical education. If this interpretation of the article was correct, it was curious that Mr. Alexander's claims to prevent disease bulked so little in the article but loomed so large in the evidence for the defendants. The whole suggestion was that Mr. Alexander was dishonest; but Dr. Jokl had said under cross-examination that he had no grounds for calling him dishonest. Not a tittle of evidence had been brought for the defence on the physical side—all the big guns had been brought to bear on the medical side. Even on that side witnesses of the highest standing had given evidence that Mr. Alexander had never claimed to cure or treat in the medical sense. They had all testified to the benefits received. Against this, the defendants and their witnesses had acknowledged that they knew nothing about the practical technique on which Mr. Alexander's claims were based but were none the less prepared to say it was all nonsense. The statement that in time the Alexander technique would provide an unfailing preventive of disease was obviously, in its context, one of Mr. Alexander's dreams of the future. It was just a hypothesis, like Dr. Cluver's, that many of man's ills came from depression and worry. There was overwhelming evidence that Mr. Alexander had specifically disclaimed any attempt to diagnose or cure diseases, and that where people had gone to him for treatment or cure he had sent them off with a flea in their ear and told them that that was a matter for a doctor.

Judgment

In a fifty-page written judgment Mr. Justice Clayden analysed the evidence given in Johannesburg and on commission in England and gave his conclusions in detail. These conclusions he summarized.[3]

Mr. Justice Clayden said that the defendants had shown that Mr. Alexander was a quack in the sense that he made ignorant pretence to medical skill. They had shown that much of the physiological reasons put forward were wrong and that in its claim to cure the Alexander system constituted dangerous quackery. In these matters, however, they had misrepresented the views of Mr. Alexander. In showing how foolish were those views which he did not put forward they had in the article in *Manpower* called him much more of a quack than they were entitled to do. In addition the defendants had failed, in his view, to prove that the Alexander system could not bring about the results claimed in the improvement of health and the

prevention of disease; again, they had made matters worse by overstating the claims made for the system. Discussing next the allegation of quackery in the field of physical education, the judge said that on the facts of the case it was Mr. Alexander's claim to improve health, not the claim to cure or prevent disease, which related to physical education. The claim to improve health had not been shown to be baseless, even in the medical field. As against the finding of the court being partly in favour of the defendants, counsel for the defence argued that if it was shown that there was quackery, and dangerous quackery, that was the sting of the article and the plaintiff would not then be entitled to an award of damages. This contention was not, in his view, well founded in law. Although he did find dangerous quackery shown in some respects, that did not put an end to the plaintiff's claim on this ground. Apart from the fact that in the present case there were charges of fraud and dishonesty—even if these were confined to the fraud and dishonesty inherent in quackery—this was a case where in substance the defendants had called the plaintiff a much worse quack than they could prove to be true. Mr. Justice Clayden then cited instances in support of the contention that the justification should be as broad as the libel.

The defendants had said that there was quackery in the field of physical education and dishonest quackery in the field of medicine, both in claims to cure and in claims to prevent disease and improve health. They had proved only quackery and dishonest quackery in the sense that quackery is always dishonest in the claim to cure. Even in that regard they had made the quackery appear to be worse than it was and they had alleged dishonesty to a greater degree than would be implicit in quackery itself. In these circumstances, too, the justification was not as broad as the libel. What the defendants had proved would assist them in the question of mitigation of damages, but it did not constitute a defence to the action. There was no evidence to justify the allegations of dishonesty in the wider sense which were imputed by the article in *Manpower*.

The two other defences set up in the defendant's plea were prescription and fair comment. It had not been argued that the action was prescribed, the evidence showing that the plaintiff came to know of the article less than a year before the issue of the summons. Nor was it necessary to deal at length with the defence of fair comment. There were so many facts in the article which were not true, either in the sense that there had been misdescription of the technique or because only part of the facts had been set out, that the foundation for the defence of fair comment had not been laid.

On the plaintiff's contention that the article was published with malice on the part of Dr. Jokl, its author, the judge said: "If that question has to be considered, it is, I think, only right to say that I think the truth of Dr. Jokl's evidence, should it come into question, is a matter with which his demeanour has nothing to do. There was nothing in his demeanour in court which gave me the impression that he was being anything but truthful."

Mr. Justice Clayden concluded, therefore, that the plaintiff was entitled to an award of damages. Although the circulation of the article had been small, it had nevertheless been circulated to important and influential readers, and the circulation had not been confined to South Africa. Bearing this in mind he had to decide what damages should be awarded for a defamation which had in part been shown to be the truth but which had throughout overstepped the mark, which in a large part of its attack had not been proved to be true, and which had made additional allegations of dishonesty and criminal conduct which were not justified.

Throughout the article scathing terms were used. The article was intended to be emphatic in its showing up of what the author regarded as a real danger. When an attack was made in such terms and was not wholly justified, those responsible could not expect an award of merely nominal damages. He considered a proper award in all circumstances to be £1,000. The defendants must also pay the costs of the action, including the cost of the application to take evidence on commission and the cost of taking that evidence.

[1] *Cape Argus*, March 1, 1948.
[2] Ibid., March 3, 1948.
[3] Ibid., April 19, 1948.

Medical Notes in Parliament

RADIOACTIVE SUBSTANCES BILL

In the House of Lords on April 29 Lord HENDERSON moved the Second Reading of the Radioactive Substances Bill. The main provisions of the Bill were summarized in our issue of April 24 (p. 812).

Lord Henderson said that a Bill with the same purpose had been introduced about a year ago but was found to be capable of improvement. Improvements suggested then had now been accepted. Radioactive substances were used in industry as luminizing agents and in the manufacture of other products. Radium and radon were employed in treating certain forms of cancer. Powerful *x*-ray tubes were used industrially, for example, for testing castings. Artificial radio-elements would shortly become available and would be of immense importance as research tools and for therapeutic purposes. Possible injuries to health if these substances were handled without stringent precautions ranged from minor burns to serious illness and death. Undue exposure to radiation might have genetic effects which as yet were uncertain. A good deal had been achieved by the British *X*-Ray and Radium Protection Committee appointed over twenty-five years ago by the Medical Research Council, but its advice had not always been asked or taken.

Artificial radioactive substances would soon be available in considerable quantities. More powerful *x*-ray apparatus was being developed. The cyclotron, the betatron, and the synchrotron, though potent tools in the hands of the scientist and the doctor, added greatly to the need for protection. Parliament must protect the worker in industry or in hospitals, the patient who ran the risk of unskilled treatment, and the public at large. In the Bill the substances and apparatus concerned and the methods of protection required were left to be laid down in Regulations. It was a difficult and complicated technical matter to draw a line between dangerous and harmless amounts of radiation, and the Government must be able by Regulations to frame appropriate definitions and apply them on expert advice. Proceeding by Regulation would facilitate amendment to meet changing circumstances in a field in which new discoveries were being made daily.

Advisory Committee

Clause 6 required Ministers to appoint an Advisory Committee after consultation with appropriate organizations which would include the Medical Research Council, the Royal Society, the Physical Society, the three Royal Colleges, and the three Corporations in Scotland, the Faculty of Radiologists, the Department of Scientific and Industrial Research, and the British *X*-Ray and Radium Protection Committee. In each case the Minister concerned was required by the Bill to consult this Committee before making Regulations, which must also be published in draft form.

The Bill proposed in Clause 3 to prohibit the sale or supply to the public of medicines or toilet preparations containing more than a prescribed quantity of radioactive material, except by a doctor or dentist holding a licence for the purpose from one of the Health Ministers or by a chemist under the authority of a prescription from a licensed doctor or dentist. Clause 3 also limited the administration of radioactive substances to licensed doctors and dentists. This was proposed because the Government was advised that the dangers inherent in many of these new substances were not universally known even among members of the medical profession.

Clause 4 required anyone using irradiating apparatus emitting radiation of a strength to be defined in Regulations for medical or dental treatment to obtain a licence from the appropriate Minister. The Government knew of many unfortunate accidents the repetition of which it intended to prevent. The Clause provided for the extension of licensing to cover the use of the apparatus for diagnostic purposes if that course was advised by the expert advisory committee. This Committee would advise on the appropriate qualifications and experience on which licences were to be granted and on conditions to be attached to the grant. Both Clause 3 and Clause 4 empowered the Ministers to exempt specified classes of persons from the requirement to obtain a licence, any such exemption being dependent on consultation with the Advisory Committee.

Safety Precautions

Clause 5 empowered the Minister to make by Regulation codes of safety precautions for the protection of the public and workers in premises where radioactive substances and

irradiating apparatus were used. Regulations relating to factories in which luminizing was carried on were already in force and had been found most useful. There were other establishments for which safety precautions should be prescribed—for example, hospitals and laboratories. In addition the Minister was empowered to ensure by Regulation that radioactive waste products from factories and so on were disposed of safely. Chimneys should be heightened to ensure that dangerous smokes were dissipated; the rate and temperature at which liquid effluent was discharged should be regulated; and contaminated articles of clothing or equipment should be disposed of safely.

Clause 1 empowered the Minister of Supply to manufacture, process, and distribute radioactive substances. This would enable him to dispose of by-products from atomic energy piles as well as natural radium and radon. The Government hoped to improve the supply of radioactive substances of all kinds for medicine, research, and industry. Clause 2 gave the Minister power to control the import and export of radioactive substances, a control at present effected under a temporary Act of 1939. Lord Henderson closed by emphasizing the Government's intention to avoid unnecessary interference with science, medicine, or industry.

Lord CHERWELL said that for the last twenty-five years there had been scarcely any cases of severe injury to persons using *x* rays. When one compared the relative safety of this sort of work with the number of deaths on the road one felt that perhaps Parliament was taking unnecessary trouble. On the other hand a number of new radioactive substances were being produced and the carrying into law of some measure such as the Bill was probably justified. He was glad that the Bill introduced last year had been replaced by the new measure. The old Bill was calculated to hamstring research. This Bill laid down that nobody, unless he had a licence, was to administer a radioactive substance to human beings. On that the Minister presumably would act on the advice of the Committee. No definition was given in the Bill of "irradiating apparatus." This too would have to be decided on the advice of the Committee. He hoped the Minister would make sure that the Committee contained industrial people who used these substances and that it was not over-weighted with medical watchdogs.

Lord AMULREE said this was the first time that any form of control of the use of *x* rays had been placed upon members of the medical profession. It would now become necessary for a doctor to obtain a special permit before he could carry out certain forms of treatment. He hoped that requirement would not become a regular practice, but he admitted that the danger to patients from the use of radium and *x* rays by medical practitioners who had not been well trained and experienced in their use was very great. He had seen catastrophic instances where people had been severely damaged by radiation. The Bill said a person carrying on a hospital, a clinic, or a nursing home could possess radioactive substances. He asked whether sufficient care would be taken to ensure that matrons could not acquire radium or other radioactive substances and keep them in such a way that proper protection was not afforded. He was pleased to see that safeguards would be provided in hospitals and factories. It would be valuable to control more buildings where radioactive substances were used, although these buildings did not come under the Factories Act.

Lord HENDERSON said physicists would have proper representation on the Advisory Committee. He was not able to say whether there would be industrial representatives. It would be within the province of the Industrial Committee to make recommendations about the conditions in which stocks of radioactive substances should be held in hospitals and nursing-homes.

The Bill was read a second time without a division and was sent to a Committee of the whole house.

Personal Injuries Bill

Sir HARTLEY SHAWCROSS moved on April 23 the Second Reading of the Law Reform (Personal Injuries) Bill. He said Clause 1 abolished the notorious doctrine of common employment whereby an employer was not responsible for injuries to his servants caused by the negligence of a fellow servant. A subsequent Clause provided that in assessing the sum to be awarded to an injured workman the courts should in future take into account his loss of earnings or profits but should set against that loss one-half of the National Insurance benefit. The courts would continue to have regard to medical expenses if these had been incurred. There would be no obligation to incur such expenses after the National Health Scheme came into operation, but if they were nevertheless incurred they would rank.

The Bill was read a second time.

Criminal Justice Bill

The LORD CHANCELLOR, in the House of Lords on April 27, moved the Second Reading of the Criminal Justice Bill, into which the House of Commons had inserted a provision suspending the execution of a capital sentence for five years. In the course of the debate the BISHOP OF WINCHESTER said Parliament had experience of other measures which were hurried forward without regard to the times. The National Health Service might for a time deprive people of medical assistance with the intention of some day providing medical assistance for all. Lord OAKSEY did not think any classification of murders or of murderers would be of benefit. It was far better to leave the matter at the discretion of the Home Secretary.

When the debate was resumed on April 28 Lord TEMPLEWOOD said the Bill proposed greater facilities for medical inspection and treatment of prisoners, on the basis that penal prisoners had to be dealt with individually. Investigation of individual cases and the adoption of the method most suitable for the particular delinquent had succeeded in the Fighting Services during the war. He felt profoundly the need for this country to show its respect for the sanctity of human life. Lord READING mentioned the substitution in the Bill of the term "Broadmoor patient" for "criminal lunatic." That exemplified the tendency in this country to call things by a different name and think that thereby their character was changed.

Lord MAUGHAM predicted that if capital punishment were suspended there would in five years be practically no difference in the number of murders. The experiment would prove nothing. A large proportion of those who spoke in the House of Commons against the death penalty did so because of the method of its administration. The method was out of date, horrible, and caused hysteria among prisoners who heard that a hanging was taking place. With modern knowledge a mere prick in the arm would surely carry out the course he held, in the interest of the State, to be necessary.

Lord BALFOUR OF BURLEIGH said he found in the Bill a provision for compulsory mental and physical examination. He understood it to be a principle of common law that an accused could not be physically examined without his consent. He believed that little could be gained from a physical examination except with the co-operation of the prisoner. He felt the proposal departed from the principles of established law. It was also a new principle of law that an innocent person should be forcibly made to give a finger-print.

The Bill was read a second time and referred to a Committee of the whole House.

Industrial Injuries.—The National Insurance (Industrial Injuries) Bill was read a first time in the House of Commons on April 29.

Hospital Beds.—Sir ERNEST GRAHAM-LITTLE inquired on April 30 how many hospital beds in England and Wales would be available on the appointed day as compared with the number in 1938. Mr. BEVAN replied that the total number of beds in England and Wales at the end of 1947, the latest date for which information was available, was 533,000. The corresponding figure for 1938 so far as known was 466,000.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Field-Marshal the Rt. Hon. Jan C. Smuts will be installed as Chancellor of the University on June 10 and will afterwards confer honorary degrees, including that of D.Sc. on Sir William Wilson Jameson, K.C.B., M.D., F.R.C.P., Chief Medical Officer, Ministry of Health and Ministry of Education; on Sir Hugh Lett, K.C.V.O., C.B.E., F.R.C.S., President of the British Medical Association; and on Sir Paul Fildes, O.B.E., M.B., B.Ch., F.R.S., Director of the Department of Chemical Bacteriology, Medical Research Council. The same honorary degree will be conferred also on Sir Robert Robinson, D.Sc., President of the Royal Society and Waynflete Professor of Chemistry in the University of Oxford.

UNIVERSITY OF GLASGOW

On April 24 the degree of M.D. was conferred upon J. Hood, Colonel J. S. K. Boyd, late R.A.M.C., and R. R. Gordon.

UNIVERSITY OF EDINBURGH

Prof. Robert McWhirter, the first occupant of the recently endowed Forbes Chair of Medical Radiology, delivered his inaugural lecture in the Pollock Memorial Hall, Edinburgh, on April 28, when he was introduced by Prof. Sydney Smith, acting Principal of the University. His subject was "Some Biological Reactions to

Radiations and Radioactive Substances." He outlined the development of radiology in the treatment of disease, from the discovery of *x* rays by Roentgen in 1895 to the present work on radioactive isotopes, and discussed the importance of radiology in the study of the nature of life, with particular reference to the structure of molecules, crystals, viruses, and genes, and the influence of radiations on the modification of gene structure and hereditary characteristics. The address concluded with a stimulating prospect of future advances in our knowledge of the nature of living tissues and the control of malignant disease.

UNIVERSITY OF LONDON

A course of six public lectures on "Pharmacology and Cell Physiology" will be given in the Physiology Theatre of University College, Gower Street, W.C., by Mr. J. F. Danielli, Ph.D., D.Sc., on Thursdays, at 5.15 p.m., from April 29 to May 6, both dates inclusive. Admission is free, without ticket. Details will be published weekly in the diary column of the *Journal*.

The British Postgraduate Medical Federation of the University has awarded postgraduate travelling fellowships for 1948–9, tenable for one year, to J. B. Kinmonth, M.S., F.R.C.S., of St. Thomas's Hospital (Surgery, U.S.A. and Sweden); H. V. Morgan, M.B., B.Ch., M.R.C.P., of St. Bartholomew's Hospital (Medicine, Canada and U.S.A.); J. P. Quilliam, M.B., B.S., of King's College, London (Physiology, U.S.A.); and W. Somerville, M.D., M.R.C.P., of the National Heart Hospital (Cardiology, U.S.A. and Sweden).

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a recent meeting of the Royal Faculty of Physicians and Surgeons of Glasgow, with Prof. Geoffrey B. Fleming, President, in the chair, the following were admitted Fellows of Faculty *qua* physician: H. Baytch, J. Clark, L. D. Gardner, F. J. Hebbert, C. M. Kesson, A. B. Sclare. The following were admitted Fellows of Faculty *qua* surgeon: J. R. Aggarwal, J. A. Bentham, J. B. Jack, P. W.-C. Mao, R. M. Mitchell, J. E. Morton, R. D. Muckart, F. H. Schikkinger.

The Services

Surgeon Rear-Admiral L. F. Strugnell and Surgeon Captain J. F. M. Campbell, R.N., have been appointed Honorary Physicians to the King in succession to Surgeon Rear-Admirals C. M. Beadnell, C.B., deceased, and A. E. Malone, C.B., R.N., who has been placed on the Retired List.

Lieutenant-Colonel James Robertson Campbell Greenlees, D.S.O., has been appointed Surgeon on the staff of Officers of the King's Body Guard for Scotland, Royal Company of Archers, in succession to Surgeon Robert Alexander Fleming, M.D., deceased.

The Efficiency Decoration of the Territorial Army has been conferred upon Lieutenant-Colonels F. Evans, M.B.E. (T.A.R.O.), H. Sissons, O.B.E., and Major J. Smith, O.B.E., R.A.M.C.

The annual dinner of the Indian Medical Service will be held at the Connaught Rooms, Great Queen Street, London, W.C., on Wednesday, June 16, when Lieut.-General Sir Bennett Hance will preside. Details may be obtained from Mr. A. W. Brown, c/o Messrs. Grindlays Bank, Ltd., 54, Parliament Street, London, S.W.1.

Colonel I. G. W. Hill, C.B.E., T.D., has been appointed Honorary Colonel, No. 2 (Sc) General Hospital.

DEATHS IN THE SERVICES

Col. C. H. Reinhold writes: Not enough has been made in the short obituary notice in the *Journal* of April 17 (p. 765) of the pioneer work that Col. HENRY SMITH did in cataract surgery during the early years of the century, and the violent controversy which raged up and down India in ophthalmic circles in those days over extraction of the cataractous lens in its capsule. The operation is still widely practised in India (or was, when I left there ten years ago), and in capable hands is continuing to give good results. Just as P. J. Freyer was a pioneer of radical prostatectomy, Henry Smith was no less a pioneer in cataract surgery throughout the world, and many surgeons from Europe and America came to sit at his feet in Jullundur and carried his technique and teaching back to their own countries. But his was not a one-track mind and his originality extended into other fields of medicine. When I and my contemporaries were being taught in the medical schools of the U.K. at the turn of the century to treat shock with stimulants and were pumping strychnine into our patients, he was already advocating morphine. He was a great man and ahead of his time as a thinker. I feel I must pay this tribute to his memory as one who fell under his spell in Jullundur nearly forty years ago.

Medical News

Air Nursing Attendants

The 1st St. John (Berkshire) Air Unit consists of 19 trained air nursing attendants available for travelling with patients in Britain or abroad. They have all passed tests in airworthiness and have been trained in special duties in addition to first aid and home nursing. All are fully insured, inoculated, and in possession of passports. These duties are undertaken voluntarily, but the patients or those responsible for them are asked to pay £2 booking-fee and 10s. for each full day after the first on which the attendant is on duty in order to cover the administrative and training expenses of the unit and to reimburse the attendant for any loss of wages. The patient is also required to pay the attendant's fare and other expenses. Applications for the services of these attendants should be made to the officer in charge of the unit, Miss S. M. George, 109, Oxford Road, Reading, Berks (Tel. Reading 4147), on the appropriate form, which can be obtained from the Brigade Secretary, 8, Grosvenor Crescent, London, S.W.1.

Election Result

The result of the election caused by the death of Dr. F. McSorley (Independent) was announced recently. Mr. S. T. Irwin, F.R.C.S.Ed. (Unionist), was returned with a majority of 1,609 over his opponent, Dr. Eileen M. Hickey (Independent), as a member of the Northern Ireland Parliament representing Queen's University, Belfast.

Called to the Bar

Dr. John A. Chapel (Middle Temple) was called to the Bar on April 21.

Christie Pension of Epsom College

The conjoint committee of the Royal Medical Foundation of Epsom College invites applications for a Christie Pension of £89 per annum from medical practitioners in need of help. Candidates must be not less than 55 years of age, and must have been registered for at least five years. In addition there are available other pensions and grants of varying amounts for medical practitioners, widows, and spinster daughters, as well as scholarships, exhibitions, and grants for children of public school age. Full information and forms of application may be obtained from the secretary's office, Epsom College, Surrey.

Current Medical Periodicals

A union catalogue of the current medical periodicals in five large medical libraries in London has been duplicated on cards, thanks to a generous grant from the Medical Research Council. The catalogue has been compiled by the librarians of the British Medical Association, the London School of Hygiene and Tropical Medicine, the Medical Research Council, the Royal College of Surgeons of England, and the Medical Sciences library at University College, London. A set of the cards, which will be kept up to date, has been deposited at each of these libraries and at the Royal Society of Medicine, the National Central Library, and the British Union Catalogue of Periodicals (British Museum).

Dried Milk for Steatorrhoea

On the recommendation of his medical advisers the Minister of Food has arranged for one 20-oz. tin per week of half-cream National Dried Milk to be supplied to patients suffering from steatorrhoea, coeliac disease, or tropical sprue instead of the machine-skimmed sweetened condensed milk at present allowed. It is obtainable (3s. a tin) from the local food office.

The Nurse's Task

The Nuffield Provincial Hospitals Trust commented on the Report of the Working Party on the Recruitment and Training of Nurses as follows: "Long-term policy cannot be suitably framed or directed until an answer can be given to the fundamental question, 'What is the proper task of a nurse?' To obtain the necessary data for this definition a complete job-analysis of the work of the nurse and the other members of the health team should be undertaken forthwith." The Trust has decided to undertake that job-analysis as part of a nation-wide survey of hospital work and staffing. It will inquire into the duties of the medical, nursing, auxiliary, and domestic staffs, but pay particular attention to the nurses, for it estimates that 30,000 more nurses are urgently required.

National Health Service

The Defenders of Human Rights are organizing a discussion on the National Health Service, to be held in the Kensington Town Hall, at 8 p.m. on Wednesday, May 19. Admission is free. The professional point of view will be put by Dr. D. A. Fermont and Mr. John Bunyan. Other speakers include Dr. Letitia Fairfield, Dr. H. B. Morgan, M.P., Mr. Wilson Harris, M.P., and Mr. I. J. Pitman, M.P.

Surgeon to Lecture in Hungary

Mr. A. E. Porritt will visit Hungary to lecture on behalf of the British Council between May 16 and 29. He will speak on penicillin in surgery, gastrectomy, and injection treatment of hernia.

Association of Doctors' Wives

The Association of Doctors' Wives (Birmingham and district) has been formed under the presidency of Prof. Hilda Lloyd with the broad intention of enabling doctors' wives to meet and discuss matters of particular interest to them, and to encourage them to take an interest in municipal and public life. The annual minimum subscription is 5s. Doctors' wives in and around Birmingham may obtain information from the Secretary, Mrs. L. H. Chitnis, 353, Chester Road, Castle Bromwich, Birmingham.

Medicine in War

The Medical Research Council has issued a report entitled *Medical Research in War* (H.M.S.O., price 7s. 6d.; pp. 455). The Council was required to advise the Government during the war on a great variety of medical problems, many of them arising directly from the conditions of warfare. Its success in one field at least is revealed by the high chance of survival of a British soldier wounded in battle—93%. The report outlines the many investigations initiated and conducted by the Council. It will be discussed in a future issue of the *Journal*.

Committee on Partnerships: Evidence Invited

The committee set up recently by the Minister of Health to consider whether Sections 35 and 36 (affecting partnerships) of the N.H.S. Act need amending will receive evidence from any organization or persons directly interested. Memoranda should be submitted to the Secretary of the Committee, Ministry of Health, Whitehall, London, S.W.1, as soon as possible, and in any case before the end of May.

Physician Emigrating

Dr. H. L. Wallace, physician at the Royal Edinburgh Hospital for Sick Children and lecturer on child life at Edinburgh University, is emigrating to South Africa to help organize a health service in Natal.

Postgraduate Surgery

The Royal College of Surgeons has prepared a scheme for providing residential accommodation for postgraduate students. The local authorities have approved the plan. Reconstruction of the College will probably start this year.

Golf Competition

The Middleton and North Manchester Medical Society are holding a competition on Wednesday, May 12, at the North Manchester Golf Club. Particulars may be obtained from Dr. J. A. Strachan, 566, Broadway, Chadderton (Tel. FAI 2230).

COMING EVENTS

St. George's Hospital Medical School

Lecture-demonstrations in neurology and psychiatry will be given in the large lecture theatre of St. George's Hospital Medical School, Hyde Park Corner, London, S.W., on Thursdays, at 4.30 p.m., from May 6 to July 22, both dates inclusive. They are open, without fee, to medical practitioners and senior medical students.

Royal Medico-Psychological Association

The next quarterly meeting of the Royal Medico-Psychological Association will be held at Dublin on Wednesday and Thursday, May 12 and 13. The programme is as follows: At Royal College of Physicians of Ireland, Kildare Street, May 12, 10.15 a.m., business meeting; 11 a.m., Drs. J. Kearney and T. W. H. Weir, "Legislation and Mental Health." 2.15 p.m., Mr. John Hayward, "The Personality of Dean Swift." 5 p.m., reception at country branch of St. Patrick's Mental Hospital, at St. Edmundsbury, near Lucan, as part of the bicentenary celebrations of Swift's hospital (St. Patrick's). At Grangegorman Hospital, May 13, 10.15 a.m., Dr. J. Dunne, "A Ten Years' Survey of Physical Methods of Treatment." 2.15 p.m., Dr. H. J. Eustace, "Addiction under the Mental Treatment Act, Eire, 1945." 8 p.m., reception by the President of Eire at his residence in Phoenix Park.

Edinburgh University Club of London

The 238th dinner of the Edinburgh University Club of London will be held at the Savoy Hotel on May 20, with H.R.H. the Duke of Edinburgh as guest of honour and Sir John Anderson, P.C., M.P., in the chair. The dress for the occasion will be evening dress with decorations. Members should have received notification of the function, but any who have not are requested to communicate with the honorary secretaries, Edinburgh University Club, 12, Wimpole Street, London, W.1.

London School of Hygiene and Tropical Medicine

The annual meeting of the Court of Governors of the London School of Hygiene and Tropical Medicine will be held at the school (Keppel Street, Gower Street, W.C.) on Wednesday, May 19, at 4 p.m.

Tuberculosis Association

A meeting of the Tuberculosis Association will be held at Birmingham on Friday and Saturday, May 21 and 22. On May 21, at 2.30 p.m., at the Queen Elizabeth Hospital, a communication on "The Clinical Estimation of Cardio-respiratory Function" will be presented by Prof. W. Melville Arnott, Dr. A. G. W. Whitfield, and Dr. G. H. Armitage, and at 4.30 p.m. Dr. Francis Jarman will speak on "The Clinical Significance of Bronchial Lesions in Pulmonary Tuberculosis." At 7.30 p.m. a reception and dinner will be given by the Lord Mayor of Birmingham at the Council House. On May 22, at 9.30 a.m., at the English Theatre, The University, Edmund Street, Dr. A. Clark Penman will present a communication on "Primary Tuberculosis in the Adult"; at 10.30 a.m., Dr. J. E. Geddes and Mr. A. L. d'Abreu will discuss "Selection of Cases for Thoracoplasty"; and at 12 noon a colour film, made by Dr. Paul H. Holinger, of St. Luke's Hospital, Chicago, on "Bronchial Tumours, etc., as seen at Bronchoscopy" will be shown by Mr. Geoffrey Bateman. The annual conference of the association will be held at Belfast on June 30, July 1, 2, and 3.

New Schools

An exhibition entitled "New Schools" will be open to the general public from May 26 to June 19 at the Royal Institute of British Architects. Examples of school furniture from several European countries as well as Britain will be exhibited.

Pathological Society of Great Britain and Ireland

The meeting of the Pathological Society of Great Britain and Ireland, which had provisionally been arranged to take place in Ghent on July 9 and 10, has had to be cancelled owing to currency restrictions. The meeting will take place in the Medical School, Leeds, on the same dates.

SOCIETIES AND LECTURES

Monday

EDINBURGH UNIVERSITY: PHYSIOLOGY CLASSROOM.—May 10, 5 p.m. "*Religion and Medical Progress*," by Dr. Douglas Guthrie.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C., May 10, 6 p.m., Cinematograph films: "*Organic Disorders of the Larynx*" and "*Bronchial Neoplasms*," by Mr. Geoffrey Bateman.

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—May 10, 8 p.m. Annual general meeting. 8.30 p.m. "*The Lure of Drugs*." Annual Oration by Dr. A. H. Douthwaite.

Tuesday

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 41, Queen's Gate Terrace, London, S.W., May 11, 7 for 7.30 p.m. Annual dinner of the 51st Session of the Society.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—May 11, 5 p.m. "*The Lichenoid Eruptions, including the Neurodermatoses*," by Dr. R. M. B. MacKenna.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C., May 11, 2.15 p.m. "*The Respiratory Tract in Infectious Diseases*," by Dr. E. H. R. Harries.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHYSIOLOGY.—At Physiology Theatre, Gower Street, London, W.C., May 11, 5 p.m. "*The Physical Aspect of Speech*," by Mr. D. B. Fry, Ph.D.

Wednesday

GLASGOW UNIVERSITY: DEPARTMENT OF OPHTHALMOLOGY.—May 12, 8 p.m. "*Disturbances of the Lacrimal Apparatus*," by Dr. James Hill.

BRITISH ASSOCIATION OF PHYSICAL MEDICINE.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., May 12, 5 p.m. Discussion: "*Physical Methods in Geriatrics*," to be opened by Mr. L. Cosin and Dr. Marjory Warren.

Thursday

CHADWICK TRUST.—At University College, University Park, Nottingham, May 13, 4 p.m. "*Advances in Preventive Medicine during the War of 1939–45*," by Sir Arthur MacNalty.

EDINBURGH ROYAL INFIRMARY.—May 13, 4.30 p.m. Honyman Gillespie Lecture: "*On Abdominal Pain*," by Mr. F. R. Brown.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, London, W.C., May 13, 5.15 p.m. "*Permeability and Drug Action*," by Mr. J. F. Danielli, Ph.D., D.Sc.

Friday

ROYAL INSTITUTION, 21, Albemarle Street, London, W.—May 14, 9 p.m. "*The Role of Chemistry in Combating Tropical Diseases*," by Sir Ian Heilbron, F.R.S.

APPOINTMENTS

Air Commodore H. A. Hewat, C.B.E., M.B., Ch.B., D.T.M.&H., has been appointed Medical Adviser to the British Red Cross Society and has taken up his duties at the society's headquarters at 14, Grosvenor Crescent, London, S.W.1.

Prof. H. W. Rodgers, F.R.C.S., and Mr. J. A. W. Bingham, F.R.C.S., have recently been appointed to the surgical staff of the Belfast Hospital for Sick Children.

DEVENISH, E. A., M.S., F.R.C.S., Surgeon to Orthopaedic and Traumatic Unit, West Middlesex County Hospital.

Mr. Devenish took the London degree with honours in 1932 and the M.S. and F.R.C.S. in 1934. During the war he served as a surgeon specialist in the R.A.M.C. He has contributed papers on "Swelling of the Upper Limb following Radical Mastectomy," "Infection of the Hand," and "The Control of *Staph. aureus* in an Operating Theatre."

BEAVAN, T. E. D., M.B., Ch.B., M.R.C.P., D.C.H., Paediatrician to West Cheshire for Cheshire County Council, Chester Corporation, and Chester Royal Infirmary.

GARTSIDE, V. O. B., M.R.C.S., L.R.C.P., D.P.H., D.I.H., Deputy Medical Officer of Health, County of Oxfordshire.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Assistant Resident Medical Officer* (*Tadworth Court*), Elspeth M. Frith, M.B., B.S. *House Surgeon*, William Roe, M.B., B.S. *House Physicians*, J. A. Black, M.B., B.Ch., M.R.C.P., and F. W. Nash, M.B., B.S., M.R.C.P.

LAIDLAW, JEAN, M.B., Ch.B., Assistant Psychiatrist, Crichton Royal Mental Hospital, Dumfries.

MIDDLESEX COUNTY COUNCIL.—The following senior appointments are announced: W. Hartston, M.D., M.R.C.P., D.P.H., Deputy County Medical Officer of Health; K. R. Stokes, M.R.C.S., L.R.C.P., Medical Director, Harefield County Hospital; R. Asher, M.D., M.R.C.P., Physician, Central Middlesex County Hospital; C. H. Dunn, M.R.C.S., L.R.C.P., D.A., Senior Anaesthetist, West Middlesex County Hospital.

MINISTRY OF NATIONAL INSURANCE.—The following appointments have been made to the headquarters medical staff of the Ministry of National Insurance: *Principal Medical Officers*, F. M. Collins, Ch.M., F.R.C.S., J. M. Davidson, M.D., D.P.H., C. J. P. Grosvenor, M.B., B.Chir. *Senior Medical Officer*, W. D. T. Brunyate, D.M., D.P.H.

MURRAY, D. L., M.B., Ch.B., D.P.H., Assistant Senior Medical Officer, Sheffield Regional Hospital Board.

PHILLIPS, W. J., M.B., B.S., D.A., Honorary Consulting Anaesthetist, Royal Victoria Infirmary, Newcastle-upon-Tyne.

SHARP, C. G. KAY, M.D., Honorary Director, Contact Lens Unit, Royal Eye Hospital, London, and King's College Hospital, London.

SLORACH, J., M.B., Ch.B., D.P.M., Deputy Medical Superintendent, Park Prewett Hospital, Basingstoke.

THOMAS, J. C. S., M.R.C.P., D.P.M., Regional Psychiatrist, North-East Metropolitan Regional Hospital Board.

WILSON, J. F., M.D., Director, Pathological Department, Royal Infirmary, Sunderland.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Borthwick.—On March 10, 1948, at Fernwood House, Jesmond, Newcastle-upon-Tyne, 2, to Betty (née Flinn), wife of Dr. J. Borthwick, 25, Redewater Road, Fenham, Newcastle, a son—David James.

Franks.—On April 28, 1948, to Marjorie (née Hutton), wife of Dr. H. Franks, of Woodford and Epping, a daughter.

Illingworth.—On May 1, 1948, at Sheffield, to Cynthia Illingworth, M.B., M.R.C.P., wife of Prof. R. S. Illingworth, M.D., F.R.C.P., a daughter.

Kitchin.—On April 11, 1948, at 265, Langley Road, Slough, to Jean (née Burles), wife of Dr. A. P. Kitchin, a daughter.

Mundy.—On April 25, 1948, at Cleveland Nursing Home, Paddington, W., to Betty (née Hall), wife of Dr. P. Gordon Mundy, 152, Plashet Road, London, E., a son—Anthony Richard.

Pugh.—On April 23, 1948, at Redruth, Cornwall, to Daphne, wife of Dr. P. J. Pugh, a son—Michael James.

Stradling.—On May 1, 1948, at Central Middlesex County Hospital, to Peggy (Dr. Snow), wife of Dr. Peter Stradling, a son.

Thomas.—On April 27, 1948, to Joyce, wife of Stanley F. Thomas, M.B.E., F.R.C.S.E., of G. Udayagiri, Ganjam District, Orissa, India, a daughter—Judith Margaret.

DEATHS

Christie.—On April 25, 1948, at the Old Rectory, Stibbington, near Peterborough, William Francis Christie, M.D.Ed., formerly of Lancaster Gate, London, W.

Clark Wilson.—On April 29, 1948, at 2, Roseburn Cliff, Edinburgh, John Clark Wilson, M.D., M.R.C.P., F.R.C.S., D.P.H., aged 77.

Coltman.—On April 27, 1948, at West Middlesex Hospital, Brentford, James Bell Coltman, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., of White Lodge, Bedfont, Middlesex, aged 41.

Conran.—On April 27, 1948, Philip Crawford Conran, M.D., of Firgrove, Maresfield Park, Uckfield, Sussex, aged 63.

Fraenkel.—On April 20, 1948, Ernest Maurice Fraenkel, M.D., of 10, Devonshire Place, London, W.

Hannan.—On April 7, 1948, John Herbert Hannan, M.D., of Southport, Lancs.

Hill.—On April 29, 1948, at Croft House Rocester, Uttoxeter, Staffs, Arthur Hilary Clifton Hill, M.R.C.S., L.R.C.P., aged 60.

Ilott.—On April 26, 1948, at Bromley, Kent, Cyril Herbert Thomas Ilott, M.B., B.Ch., aged 68.

McConnell.—On April 24, 1948, at Fernbrae Nursing Home, Dundee, George McConnell, M.B., Ch.B.Ed., of The Limes, Carnoustie, Angus.

Simpson.—On April 21, 1948, Charles Shackleton Simpson, M.R.C.S., L.R.C.P., aged 87.

Simson.—On April 24, 1948, at Wanstead, London, E., James Tudhope Simson, M.B., Ch.B.Ed.

Stobie.—On April 27, 1948, at Sutton, Surrey, Prof. Harry Stobie, F.R.C.S., F.D.S.

Young.—On April 24, 1948, at 3, Frogmore Road, Market Drayton, Salop, William Arthur Bruce Young, M.D.

No. 16

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended April 17.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948 (a)	(b)	(c)	(d)	(e)	1947 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	47	3	15	3	2	81	5	19	1	—
Deaths		1	—				3	1		
Diphtheria	136	12	53	11	3	182	24	59	22	9
Deaths	2	1	—	—	1	1	—	1	—	—
Dysentery	110	30	47	—	—	46	4	16	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	—	—	—	2	—	1	—	—
Deaths		—					—			
Erysipelas			46	10	1			36	1	1
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				27					28	
Deaths	35	3	5	5	—	84	11	16	7	1
Measles*	9,681	1360	315	96	45	9,035	490	296	44	18
Deaths†			2	1	—	20	3	—	2	2
Ophthalmia neonatorum	54	1	13	—	—	64	8	10	—	—
Deaths										
Paratyphoid fever	7	—	1(A)	—	—	5	1	—	—	—
Deaths	—	—	—	—	—	—	—	—		—
Pneumonia, influenzal	639	54	8	12	2	728	39	4	16	2
Deaths (from influenza)‡	10	—	2	1	1	16	3	3	—	—
Pneumonia, primary			213	30				252	30	
Deaths	205	45		9	8		36		9	9
Polio-encephalitis, acute	1	—				1	—			
Deaths							—			
Poliomyelitis, acute	19	1	2	1	—	9	—	2	6	—
Deaths§	3	—					—			
Puerperal fever		2	11		—		—	10		—
Deaths										
Puerperal pyrexia‖	114	4	8	6	—	139	6	12	3	3
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,290	76	252	37	38	930	73	126	26	33
Deaths†			—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	2	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	9	—	—	2	—	5	1	1	4	—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	3,888	286	61	69	22	2,117	255	399	88	13
Deaths	13	2	1	—	—	16	1	6	8	4
Deaths (0–1 year)	338	53	44	25	12	528	76	82	34	20
Infant mortality rate (per 1,000 live births)						*				
Deaths (excluding still-births)	4,615	738	619	180	120	5,270	816	688	246	109
Annual death rate (per 1,000 persons living)			12·5	11·3				14·3	15·8	
Live births	8,469	1366	1062	341	259	10,532	1662	1233	492	318
Annual rate per 1,000 persons living			21·4	21·3				24·8	31·5	
Stillbirths	211	30	31			276	41	31		
Rate per 1,000 total births (including stillborn)			28					25		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Provisional Death Rates for 1947

The decline in the maternal mortality rate in England and Wales continued during 1947, resulting in a new low figure of 1.01 per 1,000 total live and still births, compared with the previous lowest rate of 1.24 in 1946. The rate per 1,000 total live and still births for deaths from abortion was 0.17.

A male rate of 593 deaths from respiratory tuberculosis per million civilian population maintains the fall that has taken place since the high figure of 795 in 1941 and 611 in 1946. The corresponding rate for females increased from 344 in 1946 to 362 in 1947. The rates for other forms of tuberculosis were 87 for males and 72 for females.

Deaths from cancer among females continued to increase, the rate per million civilian population being 1,745, compared with 1,735 in 1946 and 1,577 in 1937. The rate for males from this cause was 1,976, compared with 1,987 in 1946.

Discussion of Table

In *England and Wales* decreases in the number of notifications were recorded for measles 1,512, acute pneumonia 64, and diphtheria 19, while an increase was reported for whooping-cough 585 and scarlet fever 94.

The largest decreases in the incidence of measles were London 449, Surrey 273, Middlesex 132, Lancashire 116, and Derbyshire 114. Notifications of whooping-cough are about twice the usual average and are the highest since 1941; during the week the largest increases were Lancashire 107, London 55, and Cheshire 52.

A small rise in the incidence of scarlet fever in most areas of the country arrested the decline that occurred during the preceding five weeks. There were no local variations of any size in the returns of diphtheria.

Three cases of paratyphoid were notified from the cities of Birmingham and Dewsbury. While a fall in the notifications of dysentery was recorded in other areas a rise occurred in London from 18 to 30 (Camberwell 14) and in Yorkshire West Riding from 17 to 28. The only other large return for dysentery was Lancashire 24.

Notifications of acute poliomyelitis were 5 more than in the preceding week. The only administrative districts with more than one case were Leicestershire, Barrow-upon-Soar R.D. 3, and Essex, East Ham C.B. 2.

An outbreak of gastro-enteritis in Scunthorpe, Lincolnshire, has caused the death of 13 babies under 12 months during the past five weeks.

In *Scotland* the incidence of measles decreased by 130, while small increases were reported for scarlet fever 14 and whooping-cough 16. The notifications of dysentery in Glasgow were 7 more than in the preceding week.

In *Eire* a decrease in the notifications of measles 34 and primary pneumonia 14 was recorded, while the notifications of whooping-cough increased by 34. The decrease in measles and the increase in whooping-cough were fairly general throughout the country.

In *Northern Ireland* the only change in the trends of infectious diseases was a decrease of 7 in the notifications of diphtheria.

Week Ending April 24

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,535, whooping-cough 3,727, diphtheria 179, measles 9,092, acute pneumonia 593, cerebrospinal fever 43, acute poliomyelitis 16; dysentery 252, paratyphoid 3, and typhoid 4. One case of cholera, a laboratory infection, was notified.

The Council on National Emergency Medical Service of the American Medical Association held its spring session recently and discussed medical aspects of modern warfare and its problems of sanitation and general hygiene. There were lectures on atomic, chemical, and psychological warfare. Dr. Edward L. Bortz, President of the A.M.A., said that it was necessary to collect information on the management of casualties caused by biological products and chemical agents. American medicine had never faced a greater challenge, and the A.M.A. was determined to function through its various councils in every way it possibly could for the protection of the nation's population. Dr. Wigodsky emphasized the necessity for nation-wide education about atomic energy so that people should have a factual basis for reasonable logical thought on the matter. Dr. G. F. McGinnes, vice-president for health services of the American National Red Cross, outlined the organization prepared for combating disaster. The Red Cross scheme includes the provision of medical supplies, equipment, and staff, and the establishment of shelters for victims who have had their houses destroyed.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Sarcoidosis

Q.—*What are the current views on the causation, symptomatology, and treatment of sarcoidosis? In what way does the Darier-Roussy sarcoid differ from the ordinary type?*

A.—Some of these problems were discussed at the International Conference of Physicians held in London in September, 1947. An absolute cause is not known, but many authorities regard sarcoidosis as a particular pattern of reaction in the tissues consequent upon sensitization (the term "anergic" is used) to a chronic infection. This may be a tuberculous infection in this country (leprosy, coccidioides, etc., in other countries), but the organism is not demonstrable and the Mantoux reaction is commonly negative. The skin lesions are most easily assessed, but similar infiltrations occur in other organs in relation to the reticulo-endothelial system. Focal or nodular, plaque or sheet infiltrations of a lupoid character are seen in the skin and may be observed in tonsils or be appreciated by palpation in deeper subcutaneous tissues, glands, liver, spleen, tendon sheaths, etc. They may be detected in the lungs and in the bones, especially of the hands and feet, by *x*-ray examination. A "chilblain circulation" may favour deposits about the nose, cheeks, ears, hands, and feet, producing a condition described as lupus pernio, which is nearly always associated with lesions in bones, lungs, and other tissues. In the experience of the writer and of others the response of calciferol in large dosage (100,000 units daily for an adult) is quite remarkable, but there is no constant response to other measures. The histology is markedly tuberculoid, and essentially presents masses of endothelioid cells with no surrounding infiltration or disorganization of collagen and rarely any tendency to caseation or giant-cell formation.

The so-called Darier-Roussy sarcoid is ill-named and bears no direct relationship to this syndrome. It is a variant of Bazin's disease, a gummatous tuberculous process associated with deep induration in the subcutaneous tissues and usually affecting the lower legs.

Failure to Ovulate

Q.—*What is the likely cause of failure to ovulate? Is any treatment likely to help? The patient I have in mind is a married woman of 28, with a history of apparently normal and regular periods. On being investigated for infertility she was told that an endometrial biopsy showed no secretory phase. What is the prognosis? She is very anxious to have a baby.*

A.—The cause of failure to ovulate in the absence of gross pelvic disorder is unknown, and its occurrence is so common that it can be regarded as being almost physiological. Since one cycle may be anovular, ovulation occurring in other cycles, the result of a single endometrial biopsy may be of little significance. In this case it would be desirable to repeat the endometrial biopsy during several cycles, or to instruct the patient in the keeping of charts of the daily waking temperature (vaginal, rectal, or oral) to see whether menstruation is regularly anovular. Alternatively, the estimation of the excretion of pregnanediol during the second half of several cycles might be helpful. Only when it is established beyond doubt that anovular menstruation occurs so commonly that it is likely to be the real cause of the infertility is treatment indicated. Treatment is in any case difficult, and the results are not easy to assess because of the ever-present possibility of a spontaneous return of ovulation.

The best hope of precipitating ovulation probably lies in the application of cyclical gonadotrophin therapy by Hamblen's technique. This consists in giving ten daily intramuscular injections of 400 units of serum gonadotrophin, followed by ten daily intramuscular injections of 500 international units of chorionic gonadotrophin. The first injection should be given

on the fifth day of a 28-day cycle (counting from the first day of menstruation). Ovulation is most likely to occur after the first or second injection of chorionic gonadotrophin, and coitus should be timed accordingly. Treatment should not be given over more than two consecutive cycles. If pregnancy does not occur the treatment should be repeated only after an interval of several months.

Thiopentone and Laryngeal Spasm

Q.—*In actual practice is there any great danger of laryngeal spasm from inducing anaesthesia with intravenous thiopentone ("pentothal") and following up with ethyl chloride and open ether? Would you use this method in the absence of a machine?*

A.—Most anaesthetists have the impression that thiopentone increases the liability to laryngeal spasm during induction of anaesthesia. As is the case with most respiratory depressants, a spasm once initiated relaxes but slowly. To minimize the risk of spasm the induction dose of thiopentone should be kept to a minimum and the subsequent ethyl chloride and ether should be administered with the same skill and artistry as though no thiopentone had been given. In these circumstances laryngeal spasm is rare. The risk of spasm is still further reduced if the larynx is sprayed with cocaine before administering the thiopentone. The thiopentone–ethyl chloride–ether sequence is quite satisfactory with the open mask. In fact, during the war thiopentone and ethyl chloride became a favourite method of induction before ether anaesthesia with the Oxford vaporizer, a method virtually equivalent to an open mask.

Repeated Haematemesis in Polycythaemia

Q.—*Can any treatment be suggested which will control repeated haematemesis and the intermittent passage of large amounts of uric acid gravel in a case of polycythaemia? Deep x-ray therapy has given only temporary benefit. Venesection once a week has helped to control the haematemesis, but has not affected the urinary condition.*

A.—Repeated haematemesis in polycythaemia is usually due to peptic ulceration, which is present in about 8% of patients with this disorder; in a smaller group polycythaemia is associated with cirrhosis of the liver (Mosse syndrome). It is of importance, therefore, to determine the cause of the haemorrhage in this particular instance and, if peptic ulceration is present, to treat it on the usual medical lines. The passage of uric acid gravel is the result of the increased urinary excretion of urates accompanying the raised level of uric acid in the blood that characterizes this disease. This can be checked only by controlling the hyperplastic process itself, and the effective means of accomplishing this are irradiation of the entire skeleton, injections of nitrogen mustard, and injections of radio-phosphorus. The last-named is not yet available in this country, and the second produces only short remissions. A copious intake of water and alkalis should help to prevent the precipitation of urates.

Varicose Ulcers

Q.—*A woman aged 58 has had severe varicose ulcers of the left leg for two and a half years. Blood Kahn and W.R. are negative and the organisms responsible are a "coliform (penicillin-resistant) and Staph. aureus (penicillin-sensitive)." All the usual applications have been tried without effect. Supporting bandages make the ulcers much worse. She has had local applications of eusol, zinc oxide ointment, and penicillin cream without effect. She refuses to go to bed for three months, because she says she did so once, and when she got up again the ulcers reappeared. Should amputation be seriously considered? I would much appreciate advice concerning further treatment.*

A.—Amputation should never be considered in ulcers due to varicose veins. The first consideration is to treat the varicose veins by combined ligation and injections: if these veins are blocked the whole management of the ulcer becomes easier. If, however, there are no veins and the ulcer is due to old femoral thrombosis or deep incompetency, then supportive treatment is the only thing to try. "Elastoplast" will often succeed when applied with great tightness and with pads of adhesive felt or "sorbo" over the ulcer itself. Another way to get a good support is to keep the patient in bed during the week-end and on Monday's visiting round apply Unna's paste, renewing this bandage each time with a preliminary two-days rest in bed. Another alternative is to apply Thiersch grafts to the ulcers with the patient in bed for four weeks. After healing, appropriate support must be continued—permanently, if necessary. It may take the form of Unna's stocking, elastic bandages, or elastic stockings, according to the amount of scarring of the leg and the tendency to oedema.

Shrunken Breasts

Q.—*A woman of 35 breast-fed her second baby for eight months, then went on holiday without the child and developed much engorged breasts. She was treated first with stilboestrol and then changed to belladonna plasters and tight bandaging, which relieved the pain. There were no ill effects at the time, but now the breasts have shrunk. Can you recommend any treatment to restore her original form?*

A.—It is very unlikely that stilboestrol or belladonna plasters, etc., could have more than a temporary effect, and probably the breasts will recover spontaneously. Stilboestrol inhibits lactation by suppression of the pituitary lactation hormone, but, apart from the period of lactation, it normally has a stimulating action on breast structure. The local inunction of ung. oestradiol or stilboestrol might be tried. It is assumed that menstruation has now returned to normal and there is no evidence of wider endocrine dysfunction—e.g., delayed pituitary superinvolution.

Egg-grown Vaccinia Virus

Q.—*Has experience confirmed the impression that post-vaccinal encephalitis may be avoided by the use of egg-grown virus for vaccination instead of the usual lymph preparation? Are supplies yet available in this country?*

A.—Insufficient numbers of individuals have been inoculated with egg-grown vaccinia virus to provide any evidence regarding the risk of post-vaccinal encephalitis from such a vaccine. In one small trial by Buddingh in the U.S.A. the lesions in 9 children inoculated with vaccinia virus grown on the chorio-allantoic membrane were milder than in 10 children who received calf lymph vaccinia virus. The neutralizing antibodies were of the same titre in both groups, one month and fourteen months after vaccination. Vaccinia virus grown on the chorio-allantoic membrane of developing chick embryos is not in current use in any country so far as is known. Further trials and improvements in production are necessary before the large-scale use of such a vaccine can be considered.

NOTES AND COMMENTS

Naming Drugs.—Mr. T. C. BLACK (Menley and James, Ltd., London) writes: Mr. Lloyd (April 17, p. 757) raises a point of some interest to us. We are arranging to make supplies of "mandelamine" (which, unfortunately, must be known here as "mandamine") available in this country, and have decided to use the description methenamine mandelate. We considered anglicizing this description, but as this is a new drug and methenamine is a *B.P.* synonym we considered it preferable to retain the original American description and to shun the confusing practice to which Mr. Lloyd rightly draws attention in the last paragraph of his letter.

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